# The Journal
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## IN THIS ISSUE

### Symposium on Hypersplenism

**Hemolytic Anemia**
**Sherman R. Kaplan**

**Management of Thrombocytopenic Purpura**
**O. Whitmore Burtner**

**Hypersplenism**
**William W. Trice, Jr.**

**Roentgen Examination of Spleen**
**J. Maxey Dell, Jr.**

**Splenectomy and Accessory Spleens**
**George W. Morse**

**Pathology of Hypersplenism**
**V. Marklin Johnson**

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# CONTENTS

## SCIENTIFIC ARTICLES


Symposium on Hypersplenism, Steven O. Schwartz, M.D., Moderator ..... 327
Hemolytic Anemia, Sherman R. Kaplan, M.D. ..... 327
Management of Thrombocytopenic Purpura, A Condensed Review, O. Whitmore Burtner, M.D. ..... 330
Hypersplenism — Agranulocytosis and Miscellaneous Manifestations, William W. Trice, Jr., M.D. ..... 334
Roentgen Examination of the Spleen, J. Maxey Dell, Jr., M.D. ..... 337
Technical Aspects of Splenectomy and Location of Accessory Spleens, George W. Morse, M.D. ..... 338
Pathology of Hypersplenism, V. Marklin Johnson, M.D. ..... 341
Discussions on Symposium ..... 344


## ABSTRACTS OF MEDICAL ARTICLES


Drs. I. Perlmutter, J. Frank Wilson, Philipp R. Rezek, Milton M. Coplan, Frank M. Woods, Perry D. Melvin and Donald W. Smith ..... 350


## EDITORIALS AND COMMENTARIES


Taking Stock ..... 355
Important Court Decision in Hoxsey Cancer Case, ..... 356
Electric Vaporizing Devices for Insecticides Present Health Hazards ..... 357
The Case of Patient Versus Case ..... 357
A. M. A. Coordinating Committee Disbands, Whitaker and Baxter Resign ..... 358
Well Done, Whitaker and Baxter ..... 359
A. M. A. Clinical Session, Denver, December 2-5 ..... 359


## GENERAL FEATURES


Officers and Committees ..... 352
From Our President ..... 354
Florida Blue Shield ..... 360
Births and Deaths ..... 361
New Members ..... 361
State News Items ..... 361
Wanted — For Sale ..... 364
Component Society Notes ..... 364
Woman's Auxiliary ..... 366
Obituaries ..... 368
Schedule of Meetings ..... 381
List of County Medical Societies, Presidents and Secretaries ..... 382



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# Symposium on Hypersplenism

MODERATOR, STEVEN O. SCHWARTZ, M.D.
CHICAGO

DR. FREDERICK K. HERPEL, West Palm Beach: The afternoon session is devoted to a symposium on hypersplenism. The moderator of this program is an internationally known hematologist, Dr. Steven O. Schwartz, Director of the Hematology Laboratory, The Hektoen Institute for Medical Research, Cook County Hospital, Chicago.

The participants are Dr. Sherman R. Kaplan of Miami Beach, Dr. O. Whitmore Burtner of Miami, Dr. William W. Trice, Jr., of Tampa, Dr. J. Maxey Dell, Jr., of Gainesville, Dr. George W. Morse of Pensacola and Dr. V. Marklin Johnson of West Palm Beach. Inasmuch as the committee had only a skeleton of the symposium, I am going to anticipate as much as I am sure you are, the ramifications of this problem as they are presented. Dr. Schwartz will introduce the various physicians who are to discuss certain features of this symposium, and I will therefore introduce to you now Dr. Steven O. Schwartz of Chicago.

DR. SCHWARTZ: Thank you very much, sir. When Dr. Patterson originally approached me relative to this symposium, he and his committee had already planned this program rather comprehensively. I think we shall have many different opinions. It is traditional in hematology that every time four hematologists get together there are six opinions. The subject of hypersplenism is a most fascinating one, made more so by the fact that we are gradually broadening our concepts of what it encompasses and learning a little of fundamental mechanisms.

# Hemolytic Anemia

SHERMAN R. KAPLAN, M. D.
MIAMI BEACH

The term "hemolytic anemia" encompasses a variety of diseases, among which are included sickle cell anemia, erythroblastosis fetalis, Mediterranean anemia, the hemoglobinurias and congenital and acquired hemolytic icterus. For the purposes of this discussion, the material presented will be limited to those hemolytic anemias characterized by a "hypersplenic" mechanism.

In discussions of abnormal hematologic states, an understanding of the basic normal relationships is an essential prerequisite. Thus it is that in this portion of the seminar I should like to introduce the subject with a brief reference to the normal.

Normal blood values depend on a balance between blood destruction in the periphery and blood formation in the bone marrow. In the peripheral blood of normal persons approximately 1 per cent of the red cells are destroyed each day and simultaneously a similar amount is replaced. This latter situation is reflected by the normal reticulocyte count of approximately 1 per cent.

Hemolytic disease refers to that type of syndrome in which increased destruction of the red blood cells occurs in the peripheral blood. Normal blood values can persist in spite of increased destruction if the rate of destruction does not exceed the compensatory capacity of the marrow to replace the cells as they are being destroyed. Anemia occurs only when there is an imbalance between the blood destruction and blood regeneration. Under such a circumstance the destruction in the peripheral blood proceeds at a rate faster than the maximal regenerative power of the marrow.

Consider for a moment the pathways of normal blood destruction: When the red blood cell has

Read before the Florida Medical Association, Seventy-Eighth Annual Meeting, Hollywood, April 29, 1952.

reached the end of its life span, it is broken down in the reticuloendothelial system and the spleen into a hemoglobin and a pigment portion. The iron and protein portions of hemoglobin are retained within the body while the pigment portion is excreted into the blood stream as the normal serum bilirubin. The bilirubin is then removed via the liver into the gastrointestinal tract and then reduced and excreted as fecal urobilinogen. A portion of the latter is reabsorbed into the blood stream and re-excreted via the kidney as the normal urinary urobilinogen.

In hemolytic anemia these pathways of normal blood destruction are accelerated. Thus, more red blood cells are destroyed, the process resulting in a greater liberation of bile pigment into the blood stream, an elevation of the icteric index, and a jaundiced patient. More pigment is excreted via the liver into the gastrointestinal tract, the excretion resulting in an increased fecal urobilinogen, and concomitantly more of this is reabsorbed into the blood stream to be excreted via the kidney as an increased urinary urobilinogen. What are the evidences of increased blood regeneration? The first of these is a hyperplasia of the bone marrow, the hyperplasia involving the erythropoietic elements. Secondly, the liberation of red blood cells into the peripheral blood is greatly increased so that one may find the reticulocyte count to be as high as 50 per cent. Furthermore, the normal marrow barriers are broken down in the attempt to compensate for the loss of cells in the peripheral blood, and younger red cells may appear in the form of nucleated red blood cells.

Thus there has been defined the evidences of increased blood destruction on the one hand and the evidences of increased blood regeneration on the other. Elevation of the serum bilirubin and increased fecal and urinary urobilinogen constitute the evidences for increased blood destruction, whereas marrow hyperplasia, elevation of the reticulocyte count and the presence of nucleated red blood cells in the peripheral blood constitute the evidences of increased blood regeneration.

### Congenital Hemolytic Icterus

Congenital hemolytic icterus is the first of the "hypersplenic" mechanisms to be discussed. It is a disease which may appear in all gradations of severity. Thus one may find a seriously ill patient with an anemia of the magnitude of 800,000 red blood cells or, contrariwise, an elderly asymptomatic patient with a normal red blood cell count and hemoglobin. As the name implies, the disease is of a familial origin and is transmitted from one of the parents to a variable number of the children. The evidences of increased blood destruction and increased blood regeneration are classical. The patient is icteric and manifests an increased urinary and fecal urobilinogen. The marrow shows an erythroid hyperplasia, and reticulocytosis is a constant finding. The presence or absence of anemia is dependent only on the balance or imbalance between the rate of blood destruction and the ability of the marrow to compensate for it.

An additional feature presents itself at this point which merits some discussion. This is the spherocytic red blood cell which is a sine qua non of congenital hemolytic icterus. The normal red blood cell is a biconcave disk measuring approximately 7.5 microns in diameter. The spherocytic cell, on the other hand, is smaller, measuring approximately 6 microns in diameter, and is more like a golf ball than a biconcave disk. The differences between the two cells may be likened to a completely decompressed balloon as the normal red blood cell and a partially blown up one as the spherocytic red blood cell. The increased hypotonic fragility as seen in all states characterized by spherocytosis then becomes easily understandable. The spherocytic cell being more completely blown up than its normal component will withstand less swelling by a hypotonic solution before it ruptures than the almost completely decompressed normal red cell.

An illustration is afforded by a family with congenital hemolytic icterus, the first of whom to present himself was Kenneth, aged 10. This child entered the hospital with a severe infection of the upper part of the respiratory tract and on admission was found to have a splenomegaly extending to 5 cm. below the left costal margin, an anemia in the magnitude of 3.5 million red cells and 57 per cent hemoglobin, a reticulocytosis of 12.8 per cent and a marrow typical of hemolytic anemia. The hypotonic saline fragility was greatly increased. Two of the siblings, Kathleen, aged 9, and Russell, aged 3, were also studied and were found to have the similar criteria of hemolytic disease. Only Dianne, aged 6, exhibited normal hematologic features. The parents, too, were investigated. The father, aged 52, had worked all of his adult life as a truck driver. Yet he exhibited the classical features of hemolytic icterus, namely splenomegaly to 6 cm. below the left costal margin in the presence of a normal red blood cell count

and hemoglobin, an elevated icteric index, an increased reticulocyte count and a marrow typical of hemolytic anemia. Here, too, the hypotonic saline fragility was greatly increased.

The therapy of congenital hemolytic icterus is splenectomy. This produces uniformly successful results, thus intimately involving the spleen in the pathogenesis of the disease. Evidences of the hemolytic syndrome disappear. This procedure was utilized in the family described with cure resulting in each instance.

### Acquired Hemolytic Icterus

The next of the hemolytic syndromes to be discussed is acquired hemolytic icterus. This disease has as its etiology a variety of considerations, among them various chemicals, infections, hemolysins and agglutinins. In addition, the acquired hemolytic anemia may be a "symptomatic" manifestation of underlying disease such as carcinoma, leukemia, lymphosarcoma, Hodgkin's disease, or other illnesses characterized by the presence of splenomegaly. The onset of acquired hemolytic anemia may be fulminating with hemoglobinuria and fever, or less severe and extending over a period of some months. The physical findings reveal the pallor and icterus with a demonstrable splenomegaly present in most of the cases. Here, too, the classic criteria of hemolytic disease are to be found, namely icterus, increased urinary and fecal urobilinogen, marrow hyperplasia, reticulocytosis, and nucleated red blood cells in the peripheral blood. Spherocytosis, too, is a feature of this disease.

Treatment of acquired hemolytic icterus consists in the main of the elimination of the noxious agent, when this is determined, and support of the patient with repeated whole blood transfusions. Splenectomy is not the treatment of choice in this disorder for it is successful in only approximately 40 to 50 per cent of the cases. It is thus held in abeyance, unless, with the elimination of all noxious agents and with the support of whole blood, the patient continues to demonstrate an unsatisfactory clinical course.

### Differential Diagnosis

It is pertinent at this point to consider the differential diagnosis between congenital and acquired hemolytic icterus, inasmuch as the classical criteria of blood regeneration and destruction are present in both and since splenomegaly and spherocytosis are features of each disease. The first point in differentiation consists of the study of the family. In congenital hemolytic icterus one or more of the family will manifest the same illness, whereas in acquired hemolytic icterus only the patient will be afflicted with the disease.

The second differential point consists in the performance of the Coombs test. This test is based upon the fact that in acquired hemolytic icterus an abnormal globulin substance coats the red blood cell in the peripheral blood, injuring it, and thus rendering it more susceptible to destruction. In congenital hemolytic icterus, on the other hand, the red blood cells are congenitally abnormal and are delivered this way directly from the marrow. The Coombs test then consists of the exposure of red blood cells from a patient with hemolytic disease to an antihuman globulin rabbit serum. If the cells exposed have been coated with the abnormal globulin substance, the combination with the rabbit serum results in the agglutination of the red blood cells, which may be detected both microscopically and macroscopically. The Coombs test thus gives positive results in most instances of acquired hemolytic icterus and always negative results in congenital hemolytic icterus.

### Summary

In conclusion then, one may state that hemolytic icterus is that type of disease characterized by increased destruction of red blood cells. This process elicits a compensatory mechanism on the part of the bone marrow to replace the cells being destroyed. The evidences of destruction are the anemia, increased serum bilirubin, a jaundiced patient, increased fecal and urinary urobilinogen, and spherocytosis. The evidences of blood regeneration are marrow erythroid hyperplasia, reticulocytosis, nucleated red blood cells in the pheripheral blood and splenomegaly.

In congenital hemolytic icterus, splenectomy is 100 per cent successful. In acquired hemolytic icterus splenectomy is successful in approximately 50 per cent of the cases, and therapy should be directed toward elimination of the noxious agents in combination with repeated whole blood transfusions. The Coombs test and study of the families of the patients are the most reliable methods of differentiating congenital and acquired hemolytic icterus.

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# Management of Thrombocytopenic Purpura
## A Condensed Review

O. WHITMORE BURTNER, M.D.
MIAMI

In this part of the symposium on hypersplenism, I should like to review, within the brief time alloted, some of the practical aspects of management of a patient with thrombocytopenic purpura in its commonly encountered forms.

Thrombocytopenic purpura due to hypersplenism is characterized clinically by petechiae and ecchymoses in the skin and spontaneous hemorrhage into mucous membranes and various tissues. The platelet count is reduced; the bleeding time is prolonged, but the blood clot does not retract; the reaction to the tourniquet test is positive; and the prothrombin consumption is decreased.

A proposed, simplified classification of thrombocytopenic purpura due to hypersplenism is shown in figure 1, and this terminology will be used in this paper. The discussion to follow will conform with the three headings of this classification, namely: (1) Idiopathic Thrombocytopenic Purpura (ITP); (2) Allergic Thrombocytopenic Purpura (ATP); and (3) Hematogenic Thrombocytopenic Purpura (HTP).

**Idiopathic Thrombocytopenic Purpura (ITP)**

Idiopathic thrombocytopenic purpura is a disease of unknown etiology, occurring most commonly in children and young adults, showing a predilection for the female sex and for the white race, and occasionally demonstrating some degree of familial incidence. The onset and course of the disease are variable, and spontaneous remissions and relapses occur.

The blood smear shows a thrombocytopenia often with variation in the size of the platelets. When severe hemorrhage has occurred, the erythrocytes may show hypochromasia and microcytosis and a temporary leukocytosis with shift to the left of the granulocytes may be present. In a case of long standing there may be a slight relative lymphocytosis and slight leukopenia.

From the Hematology Laboratory and the Department of Medicine of the Jackson Memorial Hospital.
Read before the Florida Medical Association, Seventy-Eighth Annual Meeting, Hollywood, April 29, 1952.

The bone marrow characteristically shows abnormalities of the megakaryocytes. These cells are increased in number, many of them show immaturity of the nucleus, and the cytoplasm is sometimes scanty, somewhat azurophilic, may be vacuolated, often shows fewer granules than normal and exhibits poor platelet formation. Our moderator, Dr. Schwartz,[1] was the first to direct attention to the practical, prognostic value of the bone marrow eosinophils in idiopathic thrombocytopenic purpura. He and Dr. Kaplan[2] observed that spontaneous recovery or successful splenectomy usually takes place in those cases in which there is sufficient increase in and a shift to the left of the eosinophilic granulocytes, whereas the outlook is less favorable when this eosinophilia fails to occur. I hope that we shall have the pleasure of hearing directly from Dr. Schwartz or Dr. Kaplan as to the prognostic value of marrow eosinophilia as they developed the subject at the Hektoen Institute.

Once the diagnosis of idiopathic thrombocytopenic purpura has been definitely established, consideration should be given to splenectomy in all but those cases considered mild both from the laboratory studies and on clinical grounds, in all but those in which an exacerbation of the disorder proves to be mild and transient and except in those requiring further observation to rule out the possibility of thrombocytopenic purpura due, for example, to a drug sensitivity. In general, in selecting cases for splenectomy the following factors may be important:

1. Drs. Schwartz and Kaplan have pointed out that the presence of a bone marrow eosinophilia of the metamyelocytes and myelocytes augurs for a better than usual response to splenectomy and also indicates a better than average chance for spontaneous improvement.

2. A sizable increase in platelets following the use of ACTH or cortisone would also argue for a favorable result from removal of the spleen.

**Classification of Thrombocytopenic Purpura Due to Hypersplenism**

(1) Idiopathic Thrombocytopenic Purpura (ITP)
Synonyms: "Primary," "essential," "familial" thrombocytopenic purpura.

(2) Allergic Thrombocytopenic Purpura (ATP)
Synonyms: "Secondary," "symptomatic" thrombocytopenic purpura due to certain chemical, vegetable and animal products, physical agents.

(3) Hematogenic Thrombocytopenic Purpura (HTP)
Synonyms: "Secondary," "symptomatic" thrombocytopenic purpura due to certain blood disorders and diseases associated with splenomegaly.

*Figure 1.*

3. Certainly in those patients in whom severe hemorrhage develops and who require repeated transfusions, splenectomy should be seriously considered if the diagnosis has been definitely made.

4. Operation should be given greater consideration in women than in men because of the probability of hemorrhage at menstruation and during pregnancy and because recurrences are usually more common in women than men.

5. The potential effects of idiopathic thrombocytopenic purpura should not be underrated. Even in a clinically mild form of the disease, such as in a young woman with little or no menorrhagia, if the platelet count remains consistently under 30,000 per cu. mm. with a borderline prolonged bleeding time, it is believed that splenectomy may be the best prophylaxis available against a possible cerebral hemorrhage later in life.

6. In general, it is probably fair to state that the patient who has had chronic idiopathic thrombocytopenic purpura in mild form for a long period may be expected to respond less well in terms of thrombocytosis and clinical improvement than the patient who has lived with the disorder for a shorter period, but there are exceptions to this rule.

As part of the medical treatment and in order to reduce the risk of hemorrhage associated with surgical therapy, adrenocorticotrophic hormone (ACTH) and cortisone have been tried in a limited number of cases of idiopathic thrombocytopenic purpura. Of patients so treated by Bethell, Miller and Meyers,[3] 1 patient had no remission, in 2 others the remission lasted two weeks and one month, and 4 other patients were still in remission after two weeks, four months, six months and six months, respectively. Although these hormones are worth a trial in this disease, especially when the hemorrhagic tendency is severe, it is thought that they may prove to be of even more value in allergic thrombocytopenic purpura. Transfusions of fresh whole blood, especially of platelet-rich blood, are valuable and often necessary preoperatively.

The effects of ACTH and splenectomy in a case of idiopathic thrombocytopenic purpura are illustrated in figure 2. During administration of ACTH the patient was clinically improved, the platelets slowly increased, the results of the tourniquet test became normal, the bleeding time decreased and clot retraction improved. Following splenectomy, the bleeding time and results of the tourniquet test returned almost immediately to normal, and the platelet count increased rapidly over a period of several days. An average of perhaps between 50 per cent and 80 per cent of patients with this disease may be well five years or more after splenectomy, but the reported results vary rather widely.[4-8] In some series, accessory spleens were found in as many as one third of the cases in which relapse occurred after splenectomy.[8]

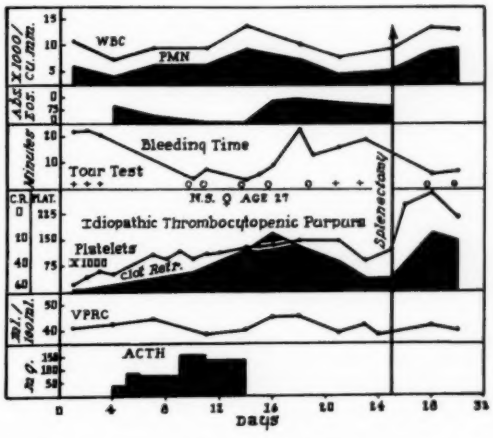


*Fig. 2. — Increase in platelet count, reduction of bleeding time and improved clot retraction, all associated with temporary clinical improvement, in a case of idiopathic thrombocytopenic purpura treated with adrenocorticotrophic hormone. The effects of splenectomy are also shown.*

Reproduced from M. M. Wintrobe: "Clinical Hematology," ed. 2, by permission of Lea & Febiger, Philadelphia.

That recent important investigations of the pathogenesis of idiopathic thrombocytopenic purpura may eventually contribute to the treatment of this disorder has been stressed in a review by Dameshek.[9]

Evans and his co-workers[9] emphasized the fact that idiopathic thrombocytopenic purpura and acquired hemolytic anemias may occur simul-

taneously in the same patient and that the Coombs test may give positive results in uncomplicated idiopathic thrombocytopenic purpura without hemolytic anemia. Using a platelet agglutination test, these workers demonstrated that this disease is due in many cases to the development of an autoimmune mechanism analogous to that present in acquired hemolytic anemia. Ackroyd[9] reported similar results in thrombocytopenic purpura due to hypersensitivity to sedormid.

Harrington[9] and his co-workers have evidence for a platelet destructive factor, possibly not originating in the spleen, which is present in the blood in some cases of idiopathic thrombocytopenic purpura. When they injected blood or plasma from patients with this disorder into patients with normal platelet counts, thrombocytopenia and a prolonged bleeding time were produced that lasted for several days, and abnormalities in the megakaryocytes of the recipient developed. In the reverse experiment, when platelets in large numbers were injected into the circulation of thrombocytopenic patients, the platelet disappearance time was considerably reduced, thus providing further evidence of a destructive mechanism.

The fact that splenectomy in idiopathic thrombocytopenic purpura often causes the megakaryocytes to produce large numbers of platelets and in some patients results in a rapid cure has led to the postulate of some form of "hypersplenism" as being responsible for this disease, either by a humoral factor acting upon the bone marrow or by excessive sequestration and phagocytosis. The fact, however, that splenectomy does not cure all patients and that the spleen appears relatively uninvolved in certain self-limited cases argues against a splenic factor being operative in every case. These recent reports should stimulate further work on a possible autoimmune mechanism being concerned in the pathogenesis of this disorder.

### Allergic Thrombocytopenic Purpura (ATP)

Allergic thrombocytopenic purpura is the acquired form of thrombocytopenic purpura regarded as being due to an allergic or sensitivity reaction,[10] especially to certain chemicals, and also at times to various vegetable and animal products and rarely to some physical agents. A partial list of these possible causative agents is shown in figure 3.

The development of purpura in an adult should arouse suspicion of reaction from a chemical agent rather than of idiopathic thrombocytopenic purpura, which is more common in childhood. Purpura due to drugs often follows the ingestion of a small dose after a short period of abstinence, although the substance may have been taken over many months without deleterious effect. This causal relationship has been well proved by test doses of sedormid,[11] sulfonamides and organic arsenicals in sensitive persons.

**Agents Reported as Causing Allergic Thrombocytopenic Purpura (ATP)**

| | | |
|---|---|---|
| (1) | CHEMICALS: | Arsenicals, sulfonamides, quinine, quinidine, sedormid, salicylates, gold salts, iodine, ergot, bismuth, tridione, streptomycin, benzol, certain organic hair dyes, phenobarbital. |
| (2) | VEGETABLES: | Foods, orris root. |
| (3) | ANIMAL: | Snake venom, pertussis vaccine, other bacterial products, insect bite, extensive burns. |
| (4) | PHYSICAL: | Heat stroke, exposure to cold. |

Adapted from M. M. Wintrobe: "Clinical Hematology," ed. 2, Philadelphia, Lea & Febiger, 1946.

*Figure 3.*

The clinical course in a patient in whom purpura develops due to sensitivity from some outside source may be highly variable. Some patients may have a purpura, without thrombocytopenia developing at any time, and this may be mild and transitory or may be more severe and subside only after several weeks. The term nonthrombocytopenic purpura has been used to describe cases of this type, and the names, Henoch's purpura and Schoenlein's purpura, have been applied when gastrointestinal symptoms and joint symptoms, respectively, are associated.

It is with the patients in whom thrombocytopenia develops at some time during the course of the purpura that we are mainly concerned in this discussion of allergic thrombocytopenic purpura. The following abbreviated report of a case illustrates some of the features of the course and management of this disorder.

### Report of Case

A 45 year old man was admitted to the Jackson Memorial Hospital for study of a mild purpura, with mild pruritis of three weeks' duration. Two weeks before the onset of the petechiae in the skin he had been given sulfadiazine in therapeutic doses by mouth over a period of three days for a mild infection of the upper part of the respiratory tract. Sulfadiazine had also been given three weeks previously for two days for a similar respiratory infection. There was a history of mild asthma ten years earlier, but the asthma had not recurred, and there was no history of hay fever, hives or food allergies. He stated that his health had always been good. No previous episode of petechiae or any easy bruising tendency had ever been noticed.

The significant findings on examination were a temperature to 99 F., small, discrete petechiae covering all of the skin areas of the body, lymph nodes essentially normal to palpation and no clinical enlargement of the liver or spleen. The hemoglobin, red blood cell count,

platelet count, bleeding time, Lee and White coagulation time and clot retraction time were all initially within normal limits, the white blood cell count was borderline elevated, an eosinophilia of 8 per cent was present, and the tourniquet test gave highly positive results after one minute.

The patient was given pyribenzamine in therapeutic doses, but became progressively worse. The petechiae became much more numerous, and some coalesced to form frank purpuric spots. He became slowly but progressively anemic and slightly jaundiced and was given blood transfusions at decreasing intervals. The spleen tip was felt two weeks after admission, and the spleen slowly and progressively enlarged. A slight generalized adenopathy of the superficial lymph nodes developed. Six weeks after admission, the patient was spiking a temperature to 103 F.; the spleen was down 5 fingerbreadths below the left costal margin; the blood transfusion requirement was about 500 cc. every 10 days, and several febrile transfusion reactions had occurred; the platelet count was down to 20,000 per cu. mm., having commenced a progressive fall to abnormally low levels two weeks after admission; the bleeding time averaged about eight minutes from the finger; clot retraction was delayed; the serum bilirubin was elevated to 3.1 mg. per hundred cubic centimeters; the Coombs test gave positive results; the reticulocyte count was up to 6.5 per cent; there was a leukopenia of about 5,000 white cells per cu. mm. with a consistent eosinophilia of about 6 per cent, and the bone marrow was moderately hyperplastic and showed a definite increase with a shift to the left of the eosinophilic elements with a relative increase in the erythroblast series.

After further transfusions of freshly drawn whole blood, a splenectomy was performed without complication with remission of the febrile course and prompt restoration of the bleeding time and platelet count to normal. This patient was in good health and asymptomatic when last seen five months ago, corresponding to three years and two months after splenectomy.

This report suggests an allergic etiology for this disorder, in this case a sulfonamide, and illustrates the progression of the disease from a nonthrombocytopenic form, which often clears up spontaneously, to a gradually developing thrombocytopenia, and the late development of a pancytopenia, which has been previously reported.[1,2] Had ACTH or cortisone been available, it is conceivable that the process might possibly have been arrested without an operation since these hormones seem to produce their best results in this form of thrombocytopenic purpura. At the least, the use of ACTH or cortisone would have been expected to reduce the potential surgical risk by bringing about substantial improvement both clinically and in the laboratory studies. During the period while the purpura was nonthrombocytopenic, the question of splenectomy did not of course arise, but ACTH might well have been valuable, according to a recent report.[3] During the period of mild thrombocytopenia, splenectomy was withheld since the spontaneous recovery rate is generally acknowledged as being relatively high in allergic thrombocytopenic purpura due, for instance, to drug allergy. Since the thrombocytopenia became progressively acute without remission and hemolytic anemia was a complication, it was believed that, in this particular patient, splenectomy may well have been a life-saving procedure.

**Hematogenic Thrombocytopenic Purpura (HTP)**

Hematogenic thrombocytopenic purpura is the acquired form of thrombocytopenic purpura due to hypersplenism arising from certain blood disorders and other diseases associated with splenomegaly. Some of these disorders are listed in figure 4.

**Blood Disorders and Diseases Associated with Splenomegaly Reported as Causing Hematogenic Thrombocytopenic Purpura (HTP)**

(1) Leukemias: All types.
(2) Anemias: Aplastic, osteosclerotic, pernicious.
(3) Splenic Disorders: Banti's syndrome, Gaucher's disease, Felty's syndrome, congenital spherocytosis, acquired hemolytic anemia, Hodgkin's disease.
(4) Infections: Septicemia, subacute bacterial endocarditis, typhus, infectious mononucleosis, tuberculosis.
(5) Miscellaneous: Thrombotic thrombocytopenic purpura, thrombopathic thrombocytopenia, lupus erythematosis disseminatus, sarcoidosis.

Adapted from M. M. Wintrobe: "Clinical Hematology," ed. 2, Philadelphia, Lea & Febiger, 1946.

*Figure 4.*

In general, thrombocytopenia, with or without anemia and leukopenia, potentially may develop in conjunction with any disease or disorder associated with splenomegaly. A good example would be a patient with lymphatic leukemia of some years standing, with a moderately large or an especially large spleen, in whom there gradually developed an increasing thrombocytopenia and in whom at about the same time there may also have developed a slowly progressive hemolytic anemia.

In managing such a patient with hematogenic thrombocytopenic purpura, in addition to any treatment contemplated for the underlying leukemia, one has the choice, depending upon the circumstances, of (1) relying largely upon fresh whole blood transfusions if the thrombocytopenia and anemia are mild, (2) administering cortisone or ACTH in as small doses as will permit maintenance of adequate levels of the platelets and red blood cells, and (3) performing splenectomy.

Greater recognition has in recent years been given to the value of splenectomy in selected cases of thrombocytopenic purpura associated with lymphoma in which, by definition, the hematogenic thrombocytopenic purpura is due to hypersplenism and not to myelophthisis. In some such cases in which the thrombocytopenia was so severe that it could not be well controlled by ordinary means, splenectomy has often restored the platelet

count to a normal or near normal value and has usually permitted the resumption of treatment with radiation or chemotherapy.

**Summary**

Salient features of the diagnosis and management of thrombocytopenic purpura due to hypersplenism are briefly reviewed.

A case illustrating the clinical course and treatment of a patient with allergic thrombocytopenic purpura is presented.

The following classification of thrombocytopenic purpura due to hypersplenism is proposed: (1) Idiopathic thrombocytopenic purpura (ITP); (2) Allergic thrombocytopenic purpura (ATP); and (3) Hematogenic thrombocytopenic purpura (HTP).

Since management and prognosis differ considerably in each of these three varieties, exact classification of the thrombocytopenic purpura is essential in each case.

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618 duPont Building.

# Hypersplenism — Agranulocytosis and Miscellaneous Manifestations

WILLIAM W. TRICE, JR., M.D.
TAMPA

Chronologically, the search for the originator or originators of the concept of abnormal splenic activity is fraught with the usual difficulties encountered in any subject in medical literature about which there has been much controversy. While there is no particular reason from our standpoint at this moment to enter into a discussion over points of historical importance, it seems noteworthy that for nearly 100 years mention has been made of the spleen in association with pathologic states. Gretsel[1] in 1866 is credited with first using the term splenic anemia in describing cases of associated anemia and splenomegaly — a term which Banti, some 30 years later, made popular. Virchow in 1845 indicated relationship of aberrations of formed elements of the blood to the spleen by use of the term "splenomedullary leukemia." As early as 1899, Rendu and Widal, according to Dameshek,[1] suggested that leukopenia might be due to hyperactivity of an enlarged spleen. In 1919, Morawitz and Eppinger[1] suggested the term "hypersplenism" as descriptive of the activities of the spleen when associated with cytopenias. Wiseman and Doan[2,3] in 1939 attracted wide attention by their paper on "Splenic Neutropenia," as did Dameshek in 1941, and Doan and Wright in 1946.

Since 1940, the interest has been progressive in the role of the spleen in abnormal states, such as have been discussed in the two previous papers this afternoon by Drs. Kaplan and Burtner, and in the probable role of the spleen in such conditions as "agranulocytosis" (more correctly, neutropenia) and the leukopenic states, both in association with, and exclusive of, a depression in the peripheral blood of platelets and/or red blood cells.

While the scope and title of this paper limit discussion, it must be borne in mind that the picture of hypersplenism is still controversial. The issues at stake are under constant clinical and research investigation and such that conclusions

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at present must be speculative, hypothetic to a large extent, and subject to constantly changing concepts.

Certainly it seems increasingly evident that it is fallacious to assume that the spleen is, per se, the primary site of disturbance. Even the term "hypersplenism" may, in a few years, seem antiquated and a term such as "hyper-reticuloendotheliosis" be found more suitable.

The division in thinking seems largely to revolve around whether the abnormally acting spleen, that is, the hyperactive organ, phagocytizes red blood cells, white blood cells and platelets, either singly, collectively, or in combination, whether this organ elaborates a hormone or hormones which act directly on the bone marrow to prevent the discharge into the peripheral circulation of one or more of the formed elements of the myeloid tissue, or whether there is a hormonal inhibition of certain elements in the bone marrow. Evidence appears to be accumulating that hormonal influences, whether elaborated under splenic influence or with the spleen simply acting as part "end-organ" of the picture, are present which are capable of producing neutropenia, thrombopenia and anemia, or combinations of these in the peripheral blood.

Neutropenia (a decrease in the granulocytes) is the rule when splenomegaly is present. Exceptions, to be sure, are outstanding, such as certain cases of myeloid metaplasia and polycythemia. Again, however, these latter two syndromes may be part of an interrelated process manifested by myeloproliferation, as suggested by Dameshek.[1]

**Hypersplenic Leukopenia**

To mention a few disorders in which there not infrequently is encountered leukopenia, one needs only to recall such malignant processes as the leukemias exhibiting at some stage a "sub" or "aleukemic" blood picture, Hodgkin's disease and lymphosarcoma. Not infrequently benign tumors are associated with leukopenia. Gaucher's disease may also have neutropenia as part of its picture, as may disorders in which there is mechanical obstruction of the portal vein or of the splenic vein (for example, thrombosis) and in cirrhosis of the liver. Further, rheumatoid arthritis, Boeck's sarcoid, disseminated lupus erythematosis, all frequently exhibit leukopenia, as do certain infections, notably typhoid, typhus, brucellosis, tuberculosis, syphilis, subacute bacterial endocarditis at times, and others.

The importance to us from a practical standpoint is that there occurs an alteration from the normal blood picture in a myriad of seemingly unrelated disease processes which may have as a common denominator splenomegaly and unusual peripheral blood patterns.

The bone marrow studied by aspiration or biopsy usually reflects a normal or increased granulocytic production that may even be hyperactive in all elements, and therefore is not diagnostic in itself of hypersplenism.

**Hypersplenism — Hormonal**

Dr. Schwartz[4] in 1937 was the first to demonstrate the experimental production of spherocytes and circulating hemolysins in hemolytic anemia. Recently there has been direct evidence demonstrating a circulating hemolysin in peripheral blood of patients suffering from thrombocytopenic purpura.[5,6] Indirect evidence and inference lead one to suspect similar processes in cases in which leukopenia, cytopenia and neutropenia occur either singly or in combination.

**Hypersplenism — Miscellaneous**

More bizarre miscellaneous manifestations appear to be a part of this complex mechanism. For example, it is known that with emotional states the spleen has been shown to contract actively, losing volume, (Barcroft, Doan, and others,[7,8]) and concomitantly in the peripheral blood a rise of red blood cells, leukocytes (particularly neutrophils) and platelets occurs. Conversely, there is a prolonged ("permanent?") rise in the peripheral blood of lymphocytes with a relative granulopenia in the postsplenectomy state.

Among other miscellaneous manifestations which, as one may readily see, beggar enumeration, the experimental work revealing the immunoprotective effect of the intact spleen in parabiotic animals to lethal infections is interesting. Jacobson and others[7, 9-11] have rather convincing evidence of the protective effect in rabbits of the intact spleen on inhibition of antibody formation following total body irradiation of sufficient degree to alter all demonstrable hemopoietic tissue (except the protected spleen) and have postulated the presence of circulating protective, humoral (noncellular) substance elaborated by the spleen. Arrowsmith, Tyrone and Lyons[12] noted the preventive effect of major hemorrhage at the time of cesarean section by splenectomy in a patient with idiopathic thrombocytopenic purpura.

Felty's syndrome (neutropenia, splenomegaly and rheumatoid arthritis) has been shown to revert to a normal blood picture following splenectomy. The arthritis remained unchanged.[13]

Volini, Schwartz and their associates[14] followed three patients carefully who were given chloramphenicol in 3 Gm. doses per 24 hours and noted that there was, within a few days, bone marrow hypoplasia, more noticeable in the granulocytic series. They also found maturation arrest in the erythroid elements. The peripheral blood reflected these changes. According to the authors, all changes reverted to normal after the drug was stopped. One wonders in this connection whether such effect was obtained by some interference by the drug of intestinal biosynthesis and subsequent splenic or reticuloendothelial effect, or whether it was due to a direct "toxic" effect of the medication per se.

So-called "periodic (cyclic) neutropenia"[15] may well be another bizarre manifestation of hypersplenism (or "hyper-reticuloendotheliosis"). Splenectomy has been noted as producing benefit by some investigators and no benefit by others.[8,15,16] The interrelationship of so-called thrombotic thrombocytopenic purpura to the "collagen disorders" has been suggested by Meacham and others.[17]

## Hypersplenism — Diagnosis

The diagnosis of a functional disorder, and certainly the present subject represents this type, is always difficult. Splenomegaly with normal bone marrow is not sufficient; neither is abnormal bone marrow, with or without splenic enlargement.

The clinician must continue to keep before him the possibility of the development of this syndrome. He must view with suspicious watchfulness, splenomegaly, signs of intravascular blood destruction and leukopenia, whether appearing as sole findings or in combination. Reaction to the Coombs test, which, when positive, has been considered confirmatory evidence of an acquired type of hemolytic anemia,[18] has been observed to change from negative to positive several months after removal of the spleen. Trypsinated red blood cells have been found valuable by Wright and Dodd and their associates[19,20] in demonstrating incomplete hemagglutinins in differentiating between congenital and acquired hemolytic anemias. Cortisone and ACTH do not alter the direction of the Coombs reaction, even though either may exert a beneficial effect upon the intravascular hemolysis. Therapeutically, ACTH and cortisone in preparation for splenectomy or in tiding the patient over a crisis are generally accepted as valuable, if not indispensable aids in the management of the well established case.


## Summary

This fascinating and frequently occurring disorder does not appear to involve any one organ system, nor does it seemingly result from any single type of bodily insult. The picture is usually protean, and the therapy not a cure. All cases considered must be judged on individual features and splenectomy reserved for those in which the procedure seems obligatory from a life-saving standpoint. It is never wise to treat the patient on the basis of abnormal laboratory reports alone, and strict skepticism along this line should be the watchword in such cases until more is understood about the abnormal physiology involved.

It is suggested that from a descriptive standpoint, "hyper-reticuloendotheliosis" may be a more exact term than hypersplenism for the aberration of the hemopoietic system discussed in this symposium.


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620 Citizens Building.

# Roentgen Examination of the Spleen

J. Maxey Dell, Jr., M.D.
GAINESVILLE

Clinicians are fully aware of the difficulties of palpating the spleen and evaluating its size. A spleen may be enlarged but not palpable due to obesity, tense or well developed abdominal muscles, a narrow costal angle or, most often, a high diaphragm. The opposite is also true. Palpable spleens may be normal. These spleens are palpable only because of a lax abdominal wall, wide costal angle or, most frequently, a low diaphragm.

In 1946 some 300 patients were studied by posteroanterior roentgenograms of the spleen at Battey General Hospital by Klinefelter and Dell.[1] The patients should be prepared by a laxative and enemas, and the stomach should be empty. Certain criteria were established which were useful, but need some revision. These were stated as follows: The spleen is not enlarged if it is: (a) not visualized, (b) less than 5 cm. in width, and (c) less than 85 per cent the size of the kidney. The spleen is enlarged if it is: (a) more than 6 cm. in width, and (b) more than 85 per cent the size of the kidney. The spleens in the group between these two were evaluated on the basis of density. It was believed that an increase in density signified that the spleen was rotated so that the anteroposterior diameter was increased, which would infer a decrease in width. This point surely must be taken into consideration. We did not use spleen length because of the inability to visualize the upper pole. The diaphragm was shown to be a poor measuring point for the upper end of the spleen.

The ideal would be clear visualization of the outlines of the spleen and left kidney. This would be the equivalent of a height-weight chart. Because of the variations in the normal, it is believed that all spleens below 6 cm. in width, and smaller than the kidney, should be considered normal in size. Spleens over 6 cm. and larger than the kidney should be considered enlarged. The height and weight of the patient and the density of the spleen should be taken into consideration.

We observed 5 patients with small spleens in whom malaria with enlargement of the spleen developed, but the size still fell within the range of normal. These patients had small spleens normally, and if we had seen them first when the small spleens were enlarged, we would have called them normal. In this type of case the size can be determined only by serial films. Eight patients were studied at weekly intervals for one to three months. The effects of exercise, rest and food were studied, and no change in the size of the spleen was noted. Studies on patients with enlarged spleens as the result of malaria showed a definite decrease in the size of the spleen after the administration of adrenalin. These spleens returned to normal after the eradication of the malaria. This method of splenography is simple technically. It is definitely more accurate than palpation and will determine splenic size in a majority of cases.

The problem of the accessory spleen is difficult. Dr. Fred Coe kindly let me have a film showing the demonstration of an accessory spleen by thorotrast. Dr. Coe condemns the administration of thorotrast without reservation. The reason is that in injecting the thorotrast if any of the material leaks into the surrounding tissue, it produces profound effects which in 1 reported case resulted in sarcoma. It is my impression that the risk of thorotrast injection is greater than the diagnostic reward justifies. Dr. Coe stated that in his 10 year follow-up study of the thorotrast cases, no evidence of systemic damage was found. Usually the accessory spleen lies just below the lower end of the spleen.

In cases in which there is a mass in the left upper quadrant of the abdomen, the determination of the organ involved is sometimes easy. A definite notch or a typical appearance will be all the evidence we need at times to state that the mass is spleen. As a general rule, the enlarged spleen does not displace the kidney downward and certainly not laterally or forward. When needed, urograms and gastrointestinal studies are of value.

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The spleen, when enlarged, usually depresses the splenic flexure and indents the greater curvature of the stomach. Usually we can determine whether the mass in the left upper quadrant is spleen or not.

In the diagnosis of splenic enlargement there is still much to be desired. Perhaps some day a material like thorotrast will be safe. In the condition of hypersplenism the determination of enlargement of the spleen is apparently of great importance, and in a considerable number of cases a plain film of the splenic area will determine the size of the spleen accurately.

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217 South Main Street.

# Technical Aspects of Splenectomy and Location of Accessory Spleens

GEORGE W. MORSE, M.D.
PENSACOLA

Time will not permit a detailed discussion of operative technic, but there are certain technical aspects of splenectomy which perhaps should be kept in mind.

The incision used for splenectomy will vary with the individual preference of the surgeon. The longitudinal, such as the upper left rectus or paramedian or Bevan, incision is perhaps the one most often used. The transverse incision which extends from the costal margin toward the mid line is used by some. The oblique or subcostal incision or left Kocher incision is excellent in the extremely obese patient. The transthoracic incision gives excellent exposure, but in the cases under discussion today it is not a satisfactory incision as exploration for accessory spleens cannot be adequately carried out. Various combinations of these incisions have been used, perhaps the best one being that of Cole (fig. 1), who starts the incision high in the left portion of the epigastrium, extending it paramedially downward 2 to 3 inches and curving it laterally to the left and parallel to the costal cartilages. The rectus muscle is transversely divided, and enough of the muscles of the anterior abdominal wall are cut to allow adequate exposure. This incision usually results in the sacrifice of only one of the intercostal nerves, and hence no weakening of the abdominal wall will occur. All incisions are concerned, however, with the exposure of the spleen and its pedicle. This is most important in the technical removal of the spleen, for if the incision is adequate and the spleen can be separated from the stomach, the pancreas and the diaphragm and the splenic pedicle ligated under direct vision, operative and postoperative complications will be reduced to a minimum.

If, upon opening the abdomen, the stomach is found to be unduly distended, a Levin tube should be passed, as this will increase the visibility and make the dissection easier unless the spleen is easily deliverable. In cases in which the spleen is large and vascular, the tube should be left in the stomach for a few days to prevent gastric distention which may displace ligatures and lead to fatal hemorrhage.

After a rapid exploration of the abdomen in search of other pathologic conditions, one should carefully inspect and palpate the spleen in order to determine its size and mobility, and the vascularity of the adhesions. It is from information derived thereby that one decides on the proper procedure. Spleens of thrombocytopenic purpura are the easiest to remove since they are not much increased in size and are usually not adherent. If this type spleen should be present and it is not adherent and easily separated at its upper pole (fig. 2), it is probably easier for one to reflect it anteriorly, placing a hot pack up under the diaphragm and proceeding with the ligation of the pedicle. This procedure is, if possible, carried out posteriorly as the veins and tail of the pancreas

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are more easily identifiable than if approached through the anterior portion of the pedicle. One should ligate the vessels separately and doubly, rather than ligating the pedicle en masse, unless emergency bleeding has occurred. Spleens which are enlarged, as in congenital hemolytic anemia, may not be adherent; in this disease they usually are not, and may be removed in the manner described.

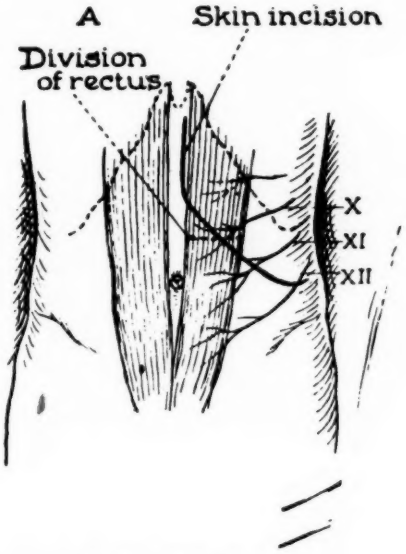


*Fig. 1.—The Cole incision.*
Courtesy, Cole, W. H. (Editor): Operative Technic in General Surgery, New York, Appleton-Century-Crofts, Inc., 1949, p. 686.

Spleens which are enlarged and adherent, as in Banti's disease, are the most difficult to remove, and it is perhaps here that a deliberate type of splenectomy should be performed. Before any attempt is made to mobilize a spleen of this type, preliminary ligation of the splenic artery is of tremendous value to the surgeon and at times life-saving to the patient (fig. 3). One can ligate it either through the gastrohepatic omentum or by detaching the gastrocolic ligament and turning the stomach upward. This procedure will expose the splenic artery, and it may be ligated near its origin from the celiac axis or it may be ligated through the floor of the lesser peritoneal cavity at the superior edge of the pancreas as it turns toward the spleen (fig. 4). This step is not alone useful in the control of hemorrhage, but in addition primary ligation of this artery will allow blood to flow out gradually from the spleen resulting in an autogenous transfusion. The vascular pressure in the spleen as well as the vascularity of the adhesions will be sharply reduced. If the ligation is performed along the superior border of the pancreas, care should be taken that the splenic vein is not ligated or torn. If it is ligated, the advantages of autogenous transfusion and decrease in vascular pressure will be lost, and if the vessel is torn, troublesome bleeding will occur. Following the preliminary ligation of this artery, the lesser peritoneal cavity is widely opened, and all the vascular and ligamentous attachments should be carefully isolated and a ligature passed around them on an aneurysm needle under direct vision before any attempt is made to deliver the spleen.

In certain cases, because of the patient's condition and the denseness of the adhesions to the diaphragm, Rives, cited by Thorek, advised separation of the parietal peritoneum from the lateral abdominal wall and diaphragm (fig. 5). This is accomplished by displacing the spleen as far as possible medially after division and ligation of all of the adhesions that can be visualized have been done. The parietal peritoneum is then divided along an irregular line anterior to the remaining attachment. Thereby a line of cleavage is opened up that is relatively avascular, and the parietal peritoneum can be stripped easily

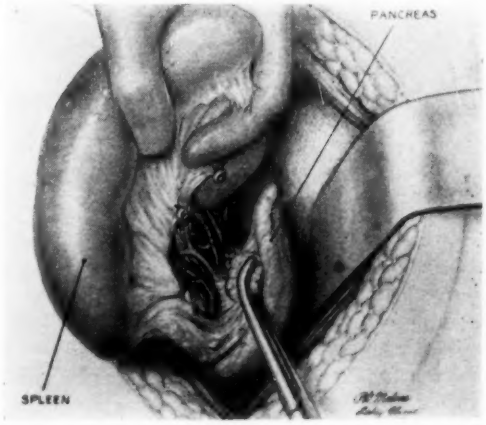


*Fig. 2.—The spleen has been reflected anteriorly and the vessels of the splenic pedicle exposed.*
Courtesy, Lahey, F. H.: Surgical Practice of the Lahey Clinic, Philadelphia, W. B. Saunders Company, 1951.

from the abdominal wall with the spleen. One should remember in dealing with this type of spleen that a large part of the bleeding which occurs during avulsion of adhesions comes from lacerations of the spleen, which tears more easily than the parietal peritoneum, and also many if not

all of the veins in the adhesions do not empty into the vessels of the abdominal wall or diaphragm but course around the spleen's surface towards the pedicle.

At times, in patients who are bad risks and in questionable operative condition, with inadequate blood bank facilities available, ligation of the splenic artery near its origin from the celiac axis is all that can be safely done. Except in patients with a ruptured spleen or in a critical condition, time is not as important, however, as to have a dry field.

With few exceptions, an adequate amount of blood should be available during the operative procedure, though in certain conditions such as congenital hemolytic anemia, it is advisable that the transfusion be delayed until the pedicle has been ligated in order to prevent hemolytic crises from occurring.

Lastly, perhaps in regard to the actual technic of splenectomy, particularly in cases of congenital hemolytic icterus or primary thrombocytopenic purpura, one should be especially careful not to handle the spleen roughly. Seeding peritoneal implants by rough handling and tearing of the splenic capsule during the operation has been known to occur. These may grow and give a disappointing result.

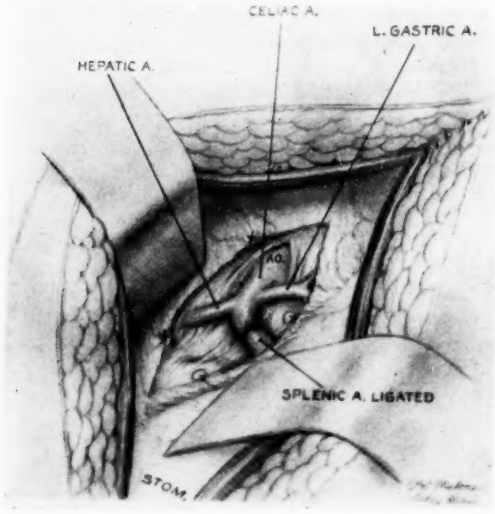


*Fig. 3.—The stomach has been displaced downward; the gastrophepatic omentum has been incised and the celiac axis exposed.*

Courtesy, Lahey, F. H.: Surgical Practice of the Lahey Clinic, Philadelphia, W. B. Saunders Company, 1951.

**Accessory Spleens**

The end result of splenectomy, particularly for congenital hemolytic anemia or primary thrombocytopenic purpura, is influenced by whether or not accessory spleens which may be present are found and removed. This factor was suggested in 1928, and subsequent observations, particularly of the accessory spleen found in recurrences after splenectomy, have aided in establishing this conclusion.

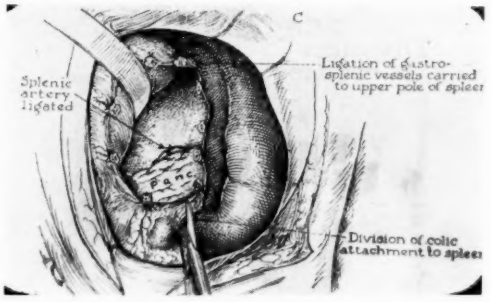
C
Ligation of gastro-splenic vessels carried to upper pole of spleen
Splenic artery ligated
Division of colic attachment to spleen

*Fig. 4.— The gastrocolic omentum has been detached and the lesser peritoneal cavity widely opened. The stomach is reflected anteriorly and toward the right exposing the pancreas which can be seen through the floor of the lesser peritoneal cavity.*

Courtesy, Cole, W. H. (Editor): Operative Technic in General Surgery, New York, Appleton-Century-Crofts, Inc., 1949, p. 686.

In a recent review based on 174 consecutive splenectomies and 4 abdominal explorations, Curtis and Movitz reported accessory spleens in 31.4 per cent of their cases. In these 56 patients 131 accessory spleens were found, with the number per patient varying from 1 to 10. Half of the patients presented only 1 accessory spleen. The percentage of instances was highest in the first decade and appeared to decrease with advancing age. This decrease was presumed to be due to a gradual involution and atrophy. In the 56 patients in their series in whom the accessory spleens were found, they were located in the following areas:

| Location | Per Cent |
|---|---|
| Hilar | 54.2 |
| Splenic pedicle | 25.1 |
| Omentum | 12.2 |
| Retroperitoneal region surrounding the tail of the pancreas | 6.1 |
| Splencolic ligamentary attachments | 1.5 |
| Mesentery of large and small intestines | 0.75 |
| In female, left adnexa | 0.15 |
| | 100.00 |

In 85.7 per cent of the patients the accessory spleens were found but in a single location. In no instance were they found in more than two locations in the same patient. If accessory spleens

*Fig. 5.—The fingers are displacing the spleen medially and the parietal peritoneum is being incised.*

Courtesy, Bancroft, F. W., and Wade, P. A. (Editors): Surgery of the Spleen in Surgical Treatment of the Abdomen, Philadelphia, J. B. Lippincott Company.

are left behind at the time of splenectomy, they can cause a recurrence of the primary splenic disease. In all cases, particularly in thrombocytopenic purpura and congenital hemolytic anemia, the surgeon should diligently look for and remove these accessory spleens.

In conclusion, in my opinion no surgeon should perform a splenectomy except in the case of a ruptured spleen without the wise judgment of the internist and the laboratory specialist.

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The Medical Center Clinic.

# Pathology of Hypersplenism

V. Marklin Johnson, M.D.
West Palm Beach

Since removal of the spleen is usually attended by dramatic clinical improvement and a striking restoration of the blood picture to normal or near normal in a variety of conditions which exhibit a diminution of one or more of the formed blood elements, these conditions have been termed varieties of hypersplenism. The term implies an abnormal increase in splenic function. At the present time there is no general agreement as regards the pathogenesis of this increased function in the conditions termed idiopathic or essential thrombocytopenic purpura, splenic neutropenia and splenic pancytopenia. There is some agreement in respect to congenital hemolytic anemia. Attempts to correlate the morphologic pattern found in the spleens removed in cases of this disease with the pre-existing hematologic picture have also proved disappointing.

Doan[1-4] and his co-workers have for years clung doggedly to the theory of hypersequestration by the spleen of the deficient blood element or elements, while Dameshek[5,6] and his associates have championed a humoral hypothesis with the spleen elaborating a substance which inhibits the proper maturation and/or release from the marrow of the deficient blood elements. Both groups have brought forth convincing evidence from their own laboratories, but attempts by others to reproduce their results have often been disappointing. Recently Wintrobe,[7] after a series of experiments on mice, expressed doubt as to the existence of any fully convincing evidence in support of either

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the concept of cell destruction or of inhibition of cell production and/or delivery in the marrow.

### The Normal Spleen

A review of the functions of the normal spleen seems pertinent at this point. Briefly these are: a reservoir for blood, an organ of erythrostasis, a lymphoid organ for production of lymphocytes and immune bodies; an organ participating in protein metabolism, a reticuloendothelial organ concerned with phagocytosis, production of monocytes, destruction of erythrocytes and formation of bilirubin, perhaps important in fat and protein metabolism, and a potential blood-forming organ. It probably exerts a control over the emission, enucleation and thickness of the red blood cells. Dameshek[8] stated that it probably controls the emission of granulocytes and may also control the formation of platelets from megakaryocytes. It is not an indispensable organ, but its removal is followed by leukocytosis, increased number of platelets, anemia or polycythemia, and such changes in the red blood cells as the appearance of target cells, Howell-Jolly bodies, and decreased osmotic fragility.

The normal weight of the spleen in the adult is approximately 150 Gm., although this will vary somewhat with its degree of engorgement. In the hypersplenic states its weight is always increased, although at times the increase may not be especially great. In essential thrombocytopenic purpura, as pointed out by Schwartz[9] and others, it seldom exceeds 300 Gm.; this is an important clinical finding, aiding in the differential diagnosis from other thrombocytopenic states. Its gross appearance, except in congenital hemolytic icterus, is not usually distinctive; in that condition, however, it is always firm and rubbery, usually having a smooth capsule and presenting an extremely dark red, almost black, cut surface, in which the splenic follicles are inconspicious. In the secondary hypersplenic states its appearance is usually characteristic of the primary disease causing the splenomegaly.

Logically one might expect to find the explanation of the increased splenic function by a study of its cellular components. Histologic studies were first concerned with its vascular supply and for years a controversy was waged as to whether it was an open or closed system. Today, as stated by Klemperer,[10] there is general agreement that it is open, but that under variable conditions the stomas of arterial terminations and of venous sinuses, as well as the grid of the reticulum mesh may become so small as to reduce it to a virtually closed one. The cellular components found in the spleen may be divided into those forming the capsule and trabeculae, those of the framework of the pulp, those of the blood vessels, and the free cells. Most attempts to explain splenic hyperfunction have centered about studies of the cells comprising the framework of the pulp and the free cells. Only in comparatively recent years has much attention been focused upon the lymphoid follicles and the perifollicular zone of adjacent cells.

The pulp is made up of a cytoplasmic reticulum and a fibrillar reticulum within which lie the cells and plasma. There is agreement that even in the adult spleen, the cytoplasmic reticulum retains its embryonal potentialities and may under different stimuli differentiate along four possible lines, namely, to form hematic, phagocytic, fibroblastic and endothelial elements. The free cells of the spleen are lymphocytes, monocytes, histiocytes (macrophages), and myeloid elements. The lymphocytes include small, intermediate and large forms, the small types predominating. The monocytes are identical with those of the peripheral blood and probably originate from the splenic reticulum. Among the phagocytic cells are erythrophagocytes and pigment cells.

The red pulp is normally the site of erythrostasis.

The white pulp is composed of a reticulum framework and reticuloendothelial and lymphoid cells. Two types of lymphoid follicles or malpighian corpuscles are present, namely, the primary follicles with pale center of lymphoblasts and few reticulum cells and small lymphocytes surrounded by a mantle zone of small lymphocytes and a marginal zone of large lymphocytes with intermingled red cells, and few mononuclear cells; the secondary follicles exhibit centers of small lymphocytes and are compact bodies lying in the reticulum.

### Pathologic Changes

Thus in the pathologic study of hypersplenism one must search for changes in the structure of the vascular bed, in the reticulum mesh, its cellular components and contents, in the lymphoid follicles and their reticulum, and in the free cells of the spleen.

In congenital hemolytic anemia the hematologic changes and morphologic findings in the spleen seem to offer a plausible explanation of the pathogenesis of this condition. The congenitally defective red cell of this disease with its increased

osmotic fragility is found packed within the meshes of the red pulp. The primary defect is to be found within the spherocytic erythrocytes and not within the spleen. The abnormal cell is caught within the meshes of the reticulum of the pulp, producing a picture of great engorgement while the splenic sinuses are compressed and are relatively empty; trapped in this manner, the abnormally fragile erythrocytes are destroyed rapidly owing probably to the mechanism of stasis, as outlined by Crosby.[11] The lymphoid follicles are relatively inconspicuous, but usually show lymphocytic centers and an outer mantle of larger cells (lymphoblasts).

In regard to essential thrombocytopenic purpura, splenic neutropenia and splenic pancytopenia, the morphologic changes within the spleen are not sufficiently characteristic to enable a definitive diagnosis. In all three conditions, however, there is undoubtedly a quantitative increase in reticuloendothelial elements, both within the reticulum mesh and within the perifollicular zone of the follicles. The sinusoids are usually dilated, and there is active phagocytosis of the element or elements found deficient in the circulating blood. Platelets are difficult to identify in tissue sections and are not reported as seen by most observers.

Von Hamm and Awny,[12] in a study of 134 cases of hypersplenism, included supravital cytologic technics in their analysis. They concluded that neither the supravital nor the fixed smear from the spleen can lend itself successfully to the differential diagnosis between normal and hyperactive splenic conditions. They further concluded that the process of blood destruction in the hyperplastic spleen could not be explained by the process of phagocytosis alone although some degree of phagocytosis of the element or elements lacking in the peripheral blood was usually demonstrated. They pointed out the important facts that the clinical picture can be invoked by small accessory spleens which obviously may invoke only a small phagocytic function, that chemical investigations of their own seem to point to a humoral mechanism, and that such a mechanism may exert a hemolytic and cytologic effect upon stagnant blood elements.

Other investigators have directed special attention to hyperplasia of the cells lining the splenic sinuses, as well as to changes within the follicles termed the "inversion phenomenon," in which the central portions of the follicles are composed of deep-staining small lymphocytes while the reticuloendothelial cells surround such centers. Leffler,[13] in a study of 87 cases of various types of hypersplenism, noted prominent widened marginal zones composed of "lymphoblasts" in all but 1 case and found the same change but occasionally in a control series. He regarded this finding as a significant criterion in the pathologic diagnosis.

## Summary

Considerable confusion still exists as to the pathogenesis and morphologic pathology of the hypersplenic states.

Congenital hemolytic anemia is primarily characterized by a congenitally abnormal erythrocyte; the spleen consistently exhibits a markedly engorged red pulp, the spaces of which are filled with spherocytes of this disease, and relatively empty sinuses. The lymphoid follicles are not distinctive, but may exhibit the "inversion phenomenon."

The morphologic findings in the spleen in essential thrombocytopenic purpura, splenic neutropenia, and splenic pancytopenia are not entirely characteristic and not sufficiently specific to enable a definitive diagnosis.

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513 Harvey Building.

## Discussions on Symposium

DR. STEVEN O. SCHWARTZ, summarizing: It was the plan, and it still is, that this should be an open discussion after my summary. For those of you who are bashful, it might be suggested that you send your questions up in written form, whereas those of you who are somewhat less bashful could perhaps ask your questions from the floor.

It is difficult to summarize so much material in two minutes and it may take me three. First, I think that we will all agree that most people have a spleen. That, I believe, is a statement we can make without too much fear of contradiction. There are exceptions, of course: these include patients who have had splenectomies and those with severe sickle cell anemia whose spleens have atrophied. There might even be an occasional congenital absence of the spleen.

Secondly, I think we will all agree that the spleen does something. Apparently, from the discussion we heard, that something is not always good. In fact, we may go so far as to say that it is bad. I think we will all agree that whatever this bad thing is that the spleen does is open to many interpretations. There is the Doan school, which is the hypersequestration school, and in that school apparently there are some dissenting voices. I imagine von Haam will be looking for a new job at the end of the academic term. There is the other school, which is the Eastern Seaboard school, and therefore a much better school, that of Dameshek. He believes that the spleen produces a hormone or a hormone-like substance which behaves primarily in an inhibitory fashion. And there is Wintrobe, way on the other side of the Mississippi, so far away that it probably does not matter much, who does not believe that either school is right. Maybe next year he will propound his own theory.

The fact of the matter is that there seem to be three mechanisms whereby the spleen can and most likely does manifest its abnormal behavior. One is the hormonal or humoral mechanism, which presumably acts at the level of cellular liberation from the marrow since in most cases of hypersplenism there is what we might describe as a maturation defect in the marrow. The cells are present, they are present in large numbers, they are present in mature forms, and at that point they apparently are stopped from getting into the peripheral blood stream. A second mechanism is the actual production of a substance in the spleen or more likely, as Dr. Trice suggested, in the entire reticuloendothelial system, which acts in a destructive fashion in the peripheral blood stream. And finally there is, according to the theory of Doan, a sequestration of cells in the spleen itself.

It is interesting that in all instances of hypersplenism there is enlargement of the spleen. In idiopathic thrombocytopenic purpura this enlargement is minimal, as both Dr. Burtner and Dr. Johnson have already mentioned. In these instances, the enlargement of the spleen is usually of a magnitude less than 100 per cent; in other words, the spleen is usually less than 300 Gm. in size, and we are wont to question the diagnosis of idiopathic thrombocytopenic purpura in all instances in which the spleen is demonstrably enlarged by palpation. This degree of enlargement, with the spleen under 250 or 300 Gm., is not demonstrable on clinical examination except in the rare case to which Dr. Dell referred. Spleens of this size would of course be demonstrably enlarged by the x-ray technic already described.

In all other instances of hypersplenism, however, the spleen is demonstrably enlarged to palpation and, if I may beg your indulgence, sir, I believe that a good clinician should be able to feel spleens which are over 300 to 350 Gm. except in the rare patient who is tremendously obese. These spleens are almost always much larger than the 300 Gm. alluded to, and therefore demonstration of the splenomegaly should not be too difficult.

I do not think that we can overemphasize the fact that there are no ironclad rules for making a diagnosis of hypersplenism, nor can we underestimate the importance of this diagnosis in both prognosis and therapy.

Let us take the papers of the essayists one by one, as I made notes on them, and by the way these are not points either of disagreement or addition, but rather points which I think bear additional emphasis. Beginning with Dr. Kaplan's paper on hemolytic anemias, it is most important, I think, to remember that in congenital hemolytic anemia or jaundice the role of the spleen is apparently a double one. The spleen undoubtedly produces some of the hemolytic substance which plays a role—a role which I think Dr. Kaplan tended to

de-emphasize—and the spleen's removal is further curative because it is in the sinusoids of the spleen where the red blood cells are apparently destroyed most rapidly due to stasis. With this organ of stasis removed, the cell survival is just sufficiently increased to enable the patient to recover balance between blood destruction and regeneration.

In the acquired hemolytic anemias, the role of the spleen is much less important, and even in those patients in whom there is a demonstrable splenomegaly, only about one third are cured by splenectomy, about one third are benefited by splenectomy, and one third are not made any better. So in those cases the prognosis is doubtful and the risk of splenectomy consequently much greater. In all these patients, however, every effort should be made to determine the cause if possible, since the cause may lie entirely outside of the spleen in the field of chemicals, drugs, allergies, or tumors.

In the discussion of thrombocytopenic purpura by Dr. Burtner, one most important point I think was not sufficiently stressed and that is the fact that thrombocytopenia is a very serious disease which carries an over-all mortality of somewhere around 20 per cent. Any disease in which 1 patient out of 5 dies cannot be dismissed as easily as most textbooks dismiss this one. In most textbooks one reads that diagnosis is made by steps one, two, three and four, the patient is splenectomized, and one assumes that thereby the patient is cured. That is not the entire story. Unfortunately many patients are splenectomized and are not cured. I am sure that that experience is shared by Dr. Burtner. An even more distressing feature to us has been the fact that we are unable, even in retrospect, to demonstrate any difference in the patient who is cured and the one who is not cured. Whether some of these more recent studies with antibodies Dr. Burtner mentioned will cast light on the subject remains to be seen.

I was greatly interested in the particular case report which was given. The patient apparently started off with a simple allergic thrombocytopenic purpura and should have recovered after the offending agent was removed; yet the chain of events continued until the patient not only had a thrombocytopenia but a hemolytic anemia, a leukopenia and, interestingly, a splenomegaly. I wonder if later in your discussion, Dr. Burtner, you might tell us if there was anything found in that spleen, although I imagine the answer is negative since it probably would have been mentioned if there had been.

It cannot be overemphasized that the diagnosis of thrombocytopenic purpura is simply the diagnosis of a symptom, and here again every effort must be made to find the precise underlying disease in accordance with the suggested subdivisions which Dr. Burtner offered.

I do think that Dr. Trice was at a distinct disadvantage in his discussion since it is most difficult to discuss the agranulocytoses or the neutropenias alone in this group of diseases for these usually occur in various combinations. His point about the importance of careful critical clinical evaluation of the individual patient bears repetition. I think Dr. Trice was being most kind in avoiding any reference to Doan's adrenalin test. I think he was being gracious to me as a guest — perhaps more so than was really necessary. As you undoubtedly know, Doan proposed that one can prognosticate the results of a splenectomy from his adrenalin test. Many of us have been performing the adrenalin test, or at least did so long enough to have become discouraged by it. Since coming down here I have learned that a new sentence has been added to the way the test should be done, which I think is important even though it comes some 15 years after the introduction of the test, and that is that the adrenalin must be given in quantity sufficient to raise the patient's pulse. Perhaps we will go back to performing the test, raising the patient's pulse without raising our own, and will learn something new about the value of the test. It is difficult sometimes to belong or be classified as belonging to one camp or the other and yet not admit that one's pulse is raised by adrenalin.

Dr. Dell spoke about the importance of the differential diagnosis of masses in the left upper quadrant of the abdomen, and as he was discussing it, I remembered many of our cases in which, had we resorted to roentgen examination, we would not have fallen quite as flat on our faces as we did. Among masses or tumors which we somehow or other mistook for spleens have been cysts of the tail of the pancreas, cysts of the mesentery, lymphosarcoma of the stomach, retroperitoneal lymphosarcoma, hypernephroma, congenital cystic disease of the kidney, hairball of the stomach, and carcinomas of the splenic flexure. I plead guilty to all these errors of diagnosis and I am sure that most of us who see enough large masses in the left upper quadrant, unless we are meticulous in

evaluating the mass, will make similar mistakes. I think that the use of roentgen examination of the abdomen of patients in whom there is a reasonable doubt as to the nature of the mass, is a most valuable contribution.

To Dr. Morse's discussion of the question of splenectomy and the operative approach, I should like to add just two small points, if I may, which we have learned to practice in the postoperative management of our patients. I am sure that it was only the brevity of time which prevented Dr. Morse from discussing them. In the presulfonamide and the prepenicillin era our operative mortality with splenectomy was almost prohibitive, and that of course was aggravated by the fact that transfusions of blood were not nearly as easily available as they are today. But the main cause of death was atelectasis of the lower lobe of the left lung with a consequent pneumonia. So even before the era of sulfonamides and penicillin, we introduced oxygen therapy routinely in the postoperative management of our patients and thereby reduced the mortality appreciably. Subsequently, with sulfonamide drugs available, they became part of our postoperative routine, and now we have substituted antibiotics for them. This has made a tremendous difference in the survival rate of our patients after splenectomy so that we approach the operation with relatively little trepidation even in the critically ill and highly complicated cases.

I think I should be most presumptious to comment on your remarks, Dr. Johnson.

If there are any questions, I am sure this excellent panel, composed of hematologists, a surgeon, a pathologist and a roentgenologist will tackle anything you can throw at it. Are there any questions?

The first question submitted is: What about the necessity of splenectomy in thrombocytopenia occurring in infectious mononucleosis?

There are cases reported in which splenectomy has been performed in patients with infectious mononucleosis due to thrombocytopenia. We have had 3 cases now in which thrombocytopenia was due to infectious mononucleosis, and we assumed that it was due to hypersplenism. In 1 case we worried for about three weeks before the platelets started to return to normal. In the other 2 cases we had much less time to wait. I think that by and large, unless the hemorrhages are dangerous, or unless the patient happens to be so old that cerebral vascular accidents are likely, I should manage a patient like that conservatively. By conservatively I mean possibly with ACTH although I am not sure that I would use it, possibly with blood transfusions although we are getting more and more conservative in our use of blood transfusions. We are more and more aware of the unfortunate complication of serum hepatitis following blood transfusion, and so unless we have to use blood we avoid it. But I think in any case, unless extremely severe or unless the hemorrhage were threatening life, I should certainly want the patient managed conservatively.

DR. GRETCHEN V. SQUIRES, Pensacola: In a familial thrombocytopenic purpura case (patient aged 6) with failure of response to splenectomy, should a bone marrow study which fails to reveal normal megakaryocytes preclude a further operation for accessory spleens?

DR. SCHWARTZ: Dr. Burtner, would you care to answer that, sir?

DR. BURTNER: I do not know whether I can answer the question from the information given. Dr. Schwartz, perhaps we can call on you for your comments. The patient is 6 years old, has a familial thrombocytopenic purpura and has not improved after splenectomy. The bone marrow fails to reveal normal megakaryocytes. Evidently, if this diagnosis is correct and the patient does have familial, idiopathic thrombocytopenic purpura, he either falls into the group that, for reasons as yet unknown, is not completely cured after removal of all the splenic tissue, or there may still be some splenic tissue remaining. This poses a difficult problem and one with which we should like to have our x-ray friends help us. Is there or is there not any accessory splenic tissue there? If we did have a technic whereby, with the injection of thorotrast, or preferably some substance that would not cause marrow depression, we could learn when accessory splenic tissue is present, we would be able to decide the important question of whether or not reoperation is indicated in a given patient. My first reaction is of course to be certain that we have the correct diagnosis in this case. Has the Coombs test been performed, and has a work-up been carried out for a possible associated hemolytic anemia? Have we also ruled out the allergic form of thrombocytopenic purpura, and could it be possible that there is an underlying blood disorder such as one of the lymphomas or leukemias? But if we do accept the fact that we are dealing here with idiopathic thrombocytopenic purpura, I think we have an exceedingly difficult

decision to make. Certainly we cannot, as Dr. Schwartz has pointed out, expect 100 per cent cures — far from it, perhaps 60 to 85 per cent of patients are benefited. I am going to pass this question back to you, Dr. Schwartz, and ask for your further comments.

Dr. Schwartz: May I ask whoever asked this question, what results were obtained in other members of the family? I presume that since the diagnosis of familial thrombocytopenic purpura was made in this patient, other members of the family may have had splenectomies.

Dr. Squires: This child had one sister who died of idiopathic thrombocytopenic purpura despite splenectomy.

Dr. Schwartz: Had no response?

Dr. Squires: Dr. Morse was the attending surgeon.

Dr. Morse: I did not operate on the patient.

Dr. Squires: You would have if the bone marrow had not shown an absence of megakaryocytes.

Dr. Schwartz: This is a most interesting case from the standpoint of two members of a family having thrombocytopenia. I think we should simply stick to the question, and that is "Should a marrow study which fails to reveal normal megakaryocytes preclude a further operation for accessory spleens?" By normal megakaryocytes you are speaking here quantitatively?

Dr. Squires: Both quantitatively and qualitatively. There was one abnormal megakaryocyte in four slides.

Dr. Schwartz: That certainly is quantitative. I am most skeptical about the ability of all of us west of the Alleghenies to know the difference between normal and abnormal megakaryocytes. You see, hematology is definitely sectional. The question of differentiating between normal and abnormal megakaryocytes is problematical, and it is only my reluctance to tell tales out of school that prevents me from telling a story about someone who claims that he can tell them apart. Certainly in this patient there would be no point in looking for accessory spleens. I think the defect here is in the megakaryocytes or the megakaryocyte-forming tissues of the marrow. I might be tempted to try some thorotrast in a patient such as this since the life expectancy is probably limited and since the complications which we fear from thorotrast are minimal, but from the evidence you give us, I doubt if re-exploration would help.

The only patients in whom we have ever seen re-exploration for accessory spleens of any value have been patients who have been cured of their disease and have remained well for a matter of months or years and then had a recurrence. We have re-explored a great number of patients who had thrombocytopenia and did not respond to splenectomy. We re-explored them because the obvious assumption was that accessory spleens were left behind. Some of them were re-explored and unfortunately a number were autopsied, but even meticulous search for accessory spleens was unrewarding.

Dr. Egbert V. Anderson, Pensacola: Dr. Schwartz, what is the opinion of the panel as to the efficacy of ACTH and/or cortisone in this particular case?

Dr. Schwartz: Dr. Burtner, would you care to answer this one?

Dr. Burtner: I should be glad to make a brief comment. Dr. Muriel Meyers, working in Dr. Cyrus Sturgis' laboratory, last week at the meeting in Cleveland, reported their experience with the use of ACTH in idiopathic thrombocytopenic purpura. She reported remissions for as long as 15 months, and there have been other similar remissions recorded. Remissions of this length, however, are apparently most unusual. In her paper, reporting some 25 cases I believe it was, I think the average length of remission was something like two, three or four weeks after discontinuing ACTH. I think, however, that from paper to paper, or one laboratory to another, one will get a different viewpoint towards the use of ACTH and cortisone, both in idiopathic thrombocytopenic purpura and in hemolytic anemia. We are all, however, probably going to come to the decision that ACTH and cortisone are not permanently curative, or at least we do not know of any patients so far who have been permanently cured of idiopathic thrombocytopenic purpura by them after long follow-up observation.

I think the administration of ACTH and cortisone in this case might be valuable in one respect. If there were a good response from such administration, it might possibly argue for the presence of some accessory splenic tissue, but it would not be at all conclusive on this point. One point against such a trial is of course the age of the child in relation to undesirable secondary effects that might be produced after a time by the hormone. Dr. Schwartz, would you comment further?

Dr. Schwartz: I have no further comment, sir. Does that answer the question?

DR. ANDERSON: I should like to ask just one more detail. How long does it take to get these remissions? I understand there is a delay of quite some time before these remissions appear.

DR. SCHWARTZ: Are you referring to after the administration of ACTH?

DR. ANDERSON: From the time it is started.

DR. SCHWARTZ: Do you care to answer that, Dr. Burtner?

DR. BURTNER: You answer it.

DR. SCHWARTZ: In our experience, if there is to be a remission, it occurs in a week or two. We prefer intravenous ACTH because we can give minimal amounts for maximum results and minimal side reactions. It is our feeling that unless there is response within three weeks, there will be none. That assumes that one is giving adequate doses. I think it is most important to emphasize that both cortisone and ACTH, in both hemolytic anemias and thrombocytopenic purpuras, have to be given in sufficiently large doses to produce these effects. We have seen failures, especially when we were first experimenting with depot ACTH and failed to get results. Subsequently, when we gave the drug in a form in which it was absorbed rapidly or when we changed to the intravenous route, we did get results.

The next question is: What percentage of hyposplenism occurs in relation to hypersplenism? I like all these men; I do not know to which one I should give this question. Dr. Trice, would you like to answer it? I am really not picking on you.

DR. TRICE: I do not know why I am singled out. I would be glad for you to answer that.

DR. SCHWARTZ: I can answer it very simply. I do not know. Hyposplenism we certainly have a right to postulate in those patients we have already mentioned who had no spleens, and those are the patients who had extirpation, had atrophy as in sickle cell anemia, and except for the changes which were described, after the removal of the spleen, by Dr. Johnson, there are no other symptoms. Is there any particular point that the gentleman who sent this up wanted to make? Perhaps we are missing the point of the question.

QUESTIONER: It struck me that from the vast amount of information presented in the papers discussed this afternoon, it appears that for practically everything we have in pathology we have the opposite. Also, in the endocrines we have the opposite. That is why I was moved to ask the question because I thought your experience would give at least some information in regard to the opposite condition, hyposplenism.

DR. SCHWARTZ: In answer to that I think I can go back to the points Dr. Johnson made in reference to what happens in the peripheral blood when the spleen is removed. Now that is not strictly hyposplenism in the sense in which we think of let us say hypothyroidism, because this is usually following the extirpation of an abnormal organ. Since, however, the changes that take place also occur after the removal of a normal spleen, we must assume that the targeting, the leukocytosis, the lymphocytosis, and the inadequate removal of nuclei as manifested by Howell-Jolly bodies are probably manifestations, at least gross manifestations, of hyposplenism. My guess is that since the spleen seems to be as important an organ as it is, there are other changes which must take place in the nonmorphologic elements of the blood. But most of these in time apparently correct themselves, and our explanation is that other reticuloendothelial tissues take over the normal functions of the spleen without actually developing into little spleens or spleniculi.

Another request is: Discuss the mechanism of the hemolytic crisis in chronic familial hemolytic anemia. Dr. Kaplan, would you like to take this?

DR. KAPLAN: The mechanism of crisis in familial hemolytic icterus is twofold: The original description of the crisis was that of a precipitous fall in red blood cell count and hemoglobin, leukocytosis, great increase in the nucleated red blood cells in the peripheral blood and a differential count which approached a leukemoid type. In conjunction with this, there was advocated the idea of a superhyperplasia of the marrow in an attempt to compensate for a superimposed peripheral destruction. More recently, however, by Dr. Owren and by others in different parts of the United States it has been advocated that the crisis of familial hemolytic icterus is not a hyperplastic crisis at all, but that initially as a result of infection or other provocative causes, there is a suppression of red cell formation in the marrow, and rather than being called hyperplastic crisis, this has been called aplastic crisis. These hematologists have shown excellent marrow preparations in which a full marrow becomes an empty one in so far as the red cell elements are concerned. You will recall the fact that in congenital hemolytic icterus the red cell survival time is considerably less than normal, that is considerably less than 100 days. Thus in a period of four or five days with abrupt cessation of red cell output from the marrow, these cells which survive only a short period of time will precipitously die off and the

red cell count and hemoglobin precipitously fall. So the concept of the mechanism of crisis in hemolytic anemia now has to be somewhat tempered with the idea that perhaps most of the crises that occur are observed five days or more after they initially appear, at a time when the marrow is then compensating for the aplastic situation which originally presented itself, and that part of what have been referred to as hyperplastic crises are really aplastic situations with initial suppression of red blood cell formation. There have been opportunities, in families of congenital hemolytic icterus where one child will develop an infection and it would be anticipated that others would incur the same infection, for a study of the marrow and peripheral blood of the sibling, and this idea of aplastic crisis has been confirmed. Sometimes the crisis is precipitated by an attack of cholecystitis, a frequent cause. Cholelithiasis, as you know, is extremely common in congenital hemolytic icterus since there is an overwhelming passage of bile through the biliary tract. Not infrequently a nidus forms and pigment stones occur, and an attack of biliary obstruction from stone or infection from stasis may provoke an attack of hemolytic crisis.

Dr. Schwartz: This question has been submitted: Would you expect any benefit from cortisone or ACTH in pancytopenia due to myelophthisis? Would you care to answer that, Dr. Trice?

Dr. Trice: The appearance of depression peripherally of the formed elements of the blood in the myelophthisic anemias or invasion anemias produced by invasion of the bone marrow has been of course investigated under the name of aplastic anemia. Really it is hypoplasia of all the formed elements of course, and its response to cortisone and ACTH has been extremely disappointing, even in marrow sections followed serially over a period of months. The expectation of any benefit from cortisone or ACTH in this type of anemia is, I am sure, beyond reason. It is too much to expect even of the miracle drugs.

Dr. Schwartz: How accurate are megakaryocyte counts on bone marrow? Dr. Burtner, would you care to answer this question?

Dr. Burtner: I am a poor choice to answer the question because I do not follow the practice of making megakaryocyte counts on bone marrow samples. I know that certain laboratories do make such counts, especially for research purposes. In my opinion a good look at a marrow smear, provided it has been made on a cover slip, gives an excellent idea (1) as to the number of megakaryocytes present, as estimated by looking through the low power objective, and (2) the quality of the megakaryocytes, studied under a higher power. In a classical case of idiopathic thrombocytopenic purpura (ITP) there is usually a considerable increase in megakaryocytes and megakaryoblasts together with evidence of immaturity of the nucleus, basophilia of the cytoplasm and poor platelet formation. It is also true, however, and a point of some confusion, that in allergic thrombocytopenic purpura (ATP), developing as a result of sensitivity to such drugs as salicylates or sulfonamides, there may be much the same picture of increased numbers of megakaryocytes with the same abnormalities of them; hence we cannot use the bone marrow as a point of differentiation between these two related disorders. I think we should not place too much emphasis on the absolute number of megakaryocytes, since we know they can be increased in a number of other conditions in which the bone marrow is stimulated or irritated.

Dr. Schwartz: The next request is: Please discuss the method you use in palpation of the spleen. Is there a willing subject in the audience? I should be happy to demonstrate on her. I think in palpating for the spleen, it is most important to assume a priori that the spleen is enlarged and then make every possible effort to prove that it is enlarged. Most of the spleens which are missed on palpation are the huge spleens which fill the left half of the abdomen. The examiner puts his hand on the abdomen, and there is no splenic edge where he expects to find it; so he dismisses the spleen. We recommend that one palpate the abdomen with as much thoroughness as one examines the chest. That is unfortunately not too often done. We also find that placing the patient on his right side with the legs drawn up, thereby relaxing the abdominal wall, helps greatly in finding spleens which otherwise are somewhat more difficult to feel. But, above all, the important thing is to assume that the patient has splenomegaly, which of course in our field is a fairly safe bet.

One point I should like to make in this connection is that we do not consider palpable spleens normal, even though every once in a while we do find, especially in younger persons, a splenomegaly which we are unable to explain. Certainly every patient with a splenomegaly is deserving of a thorough evaluation. Are there any other questions?

Dr. James N. Patterson, Tampa: Dr. Schwartz, about a year ago, Dr. Doan of Colum-

bus, who was mentioned earlier in the discussion, gave a course in Jacksonville in which he advocated the use of thorotrast in the search for accessory spleens. I wonder if Dr. Dell would tell us why he is so afraid of thorotrast.

DR. SCHWARTZ: Dr. Dell, sir.

DR. DELL: Dr. Patterson, I have had no experience with thorotrast. I would have to be guided entirely by the opinion of Dr. Coe, who has had a world of experience with it. He thought that as a general rule the diagnostic yield did not justify the risk. As Dr. Schwartz brought out, in the occasional case if it is extremely important to find the small accessory spleen, then it would probably be wise to take that risk, the risk being entirely, as far as I can gather from Dr. Coe, the extravenous extravasation of the thorotrast into the tissues. Of course you know the experiments on the ventricles of dogs and the ventricles of monkeys that have been carried out. Just as a defense about palpating the spleen versus the roentgen ray examinations, I should like to say to Dr. Schwartz that this is what makes horse races and that I believe probably the ability of the clinician to palpate spleens also has a geographic distribution.

DR. SCHWARTZ: I should probably have been a most disappointed man if there had not been at least a little controversy. Are there any other questions? If not, I should like to congratulate Dr. Patterson on bringing together so distinguished a group of participants in this symposium and to thank him for inviting me. I hope that I have adequately fulfilled my role of a moderator. Thank you.

DR. HERPEL: Thank you very much, Dr. Schwartz, and the members of this Association who have participated in this most interesting discussion. This departure from the usual procedure in setting up these scientific assemblies was done with some doubts. The attendance at this meeting and the fact that so many have stayed throughout the entire symposium furnish good evidence that there is a genuine interest in the production of such a symposium. I think I can assure you that the experiment probably will be repeated.

## ABSTRACTS OF MEDICAL ARTICLES

**Paralysis Caused by Penicillin Injection; Mechanism of Complication — A Warning.** By I. M. Tarlov, M.D., I. Perlmutter, M.D., and A. J. Berman, M.D. J. Neuropath. & Exper. Neurol. 10:158-176 (April) 1951.

Results of experiments are reported which clarify the mechanism that produces severe peripheral neuritis as an immediate complication of the intramuscular injection of penicillin. These experimental observations offer an explanation of the mechanism by which almost complete sciatic paralysis immediately followed the intragluteal injection of penicillin in a patient whose case history is presented.

This extensive investigation established that the intense and persistent neuritis, accompanied by pronounced interruption of nerve function, is attributable to the introduction of the material directly into the parenchyma of the nerve. The resultant inflammatory reactions were much more intense with the oily than with the soluble penicillin. Streptomycin injections produced similar reactions. The nerve sheaths appeared strongly to resist the inflammatory reactions and thus to protect the nerve fibers when penicillin was injected around the nerve or into its epineurial sheath. Also, hemorrhage into or around the sciatic nerve did not cause the neuritis.

Delayed impairment of nerve function, occurring after eight to seventeen days in some cases, offered the experimental counterpart of the similarly delayed onset of symptoms referable to neuritis in human cases, in which the neuritis was probably due to progressive inflammatory and fibrotic changes.

When administering penicillin or any other form of intramuscular therapy, the authors warn, one should make the injections remote from the site of any of the large nerve trunks. The chosen site for intragluteal injections should be the upper outer quadrant. In view of the danger of pulmonary embolism, it is important also to guard against the intravenous injection of the oily suspension of penicillin. Repeated aspiration of the material should be attempted during the injection.

**The Treatment of Larva Migrans with Stibanose, A Preliminary Report.** By J. Frank Wilson, M.D. South. M. J. 45:127-130 (Feb.) 1952.

In this preliminary report on the use of stibanose in the treatment of larva migrans or creeping eruption, Dr. Wilson discusses the incidence, etiology and various methods of treatment of this skin disorder, which for some years has given cause for growing concern in the coastal regions of the Southeastern United States. He notes that in Florida alone in 1950, over 7,000 cases were reported, with probably twice that number unreported.

In his series of 75 cases, treatment with stibanose effected complete cure in 30 per cent, was highly effective in 66 per cent, making the patient comfortable in approximately twenty-four hours, and was ineffective in 4 per cent. No unfavorable reactions occurred.

In view of the prevalence of larva migrans and the need for improved therapy, Dr. Wilson concludes that stibanose warrants extensive clinical trial as the treatment of choice, supplemented by topical application of ethyl acetate collodion, and freezing of individual lesions when necessary.

**Histological Studies of Carcinoma of the Prostate Treated by Estrogen.** By Philipp R. Rezek (by Invitation), Milton M. Coplan, Frank M. Woods and Perry D. Melvin. J. Urol. 66:379-389 (Sept.) 1951.

Studying hundreds of prostates surgically removed or obtained from autopsies for the past six to eight years, the authors noticed so-called squamous cell metaplasia (the transformation of columnar or cuboidal epithelium into squamous epithelium) more frequently than expected, no matter whether these glands showed benign hypertrophy, with or without inflammatory changes, prostatic infarcts, calculi, or carcinoma. In a number of these cases, the patient had received stilbesterol for one reason or another. This observation suggested studies on the histologic influence of stilbesterol on carcinoma of the prostate and its metastases.

Four cases are presented, representing similar response to estrogen in different types of cases. In the first case, clinically misdiagnosed as carcinoma, the patient received stilbesterol and was then subjected to operation. The second case was one of carcinoma, in which estrogen therapy was followed by surgery. In both of these cases the connection between metaplasia and estrogen administration, while not conclusive, appeared highly probable.

Carcinoma was present in the third case, in which orchiectomy was performed; stilbesterol therapy was continued for years, repeated biopsies were obtained and transurethral resection was performed six times. Study of the numerous biopsies showed how the pattern of the carcinoma changed under the influence of the different therapeutic procedures. It appeared highly probable that under the influence of stilbesterol the carcinoma changed its aspect completely, inasmuch as the adenocarcinoma was converted into a poorly differentiated squamous cell carcinoma.

The fourth case, one of carcinoma with metastases treated by estrogen therapy, terminated fatally, and autopsy was performed. The particular importance of this case lies in the evidence it offered that estrogen not only changes the pattern of the primary tumor but also produces metaplasia in its bone metastases, apart from well known fibrosis and osteoplasia, an anomaly believed not previously described in the literature.

It is concluded that the administration of estrogen seems to induce the changes described, which may explain its favorable effects on primary carcinoma of the prostate and its bone metastases.

**The Surgical Significance of the Cardiosplanchnic Reflex.** By Donald W. Smith, M.D., and Matthew A. Larkin, M.D. South. M. J. 44:399-407 (May) 1951.

The authors present a diagnostic aid in the differentiation between cardiac and abdominal visceral lesions in those cases in which the region of pain manifestation is misleading.

Seven cases are presented illustrating severe abdominal pain in cardiac lesions and severe precordial pain in abdominal visceral lesions. The mechanism of transfer is described as the cardiosplanchnic reflex, through an anatomic overlap of the lower cardiac nerves and the upper splanchnic nerves at the fourth and fifth dorsal segments.

A stellate block, successfully performed, will relieve or alter pain of cardiac origin regardless of where it occurs, but will not alter chest pain of abdominal or splanchnic origin. A splanchnic block, on the other hand, will promptly relieve severe pain of upper abdominal visceral origin even though it is manifest in the chest.

Methods of stellate and splanchnic block are described and illustrated which are relatively safe, and technically simple to perform.

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Edward Jelks, M.D., 1937.....*Jacksonville*
W. Henry Spiers, M.D., 1938.....*Orlando*
Leigh F. Robinson, M.D., 1939.....*Fort Lauderdale*
Walter C. Jones, M.D., 1941.....*Miami*
Eugene G. Peek, Sr., M.D., 1943.....*Ocala*
John R. Boling, M.D., 1944, 1945.....*Tampa*
Shaler Richardson, M.D., 1946.....*Jacksonville*
William C. Thomas, Sr., M.D., 1947.....*Gainesville*
Joseph S. Stewart, M.D., 1948.....*Miami*
Walter C. Payne, M.D., 1949.....*Pensacola*
Herbert E. White, M.D., 1950.....*St. Augustine*
David R. Murphey, Jr., M.D., Sec'y., 1951.....*Tampa*

# *From Our President*

## What Do You Think?

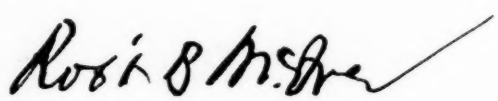
With sights set on the 1953 Annual Meeting to be held in Hollywood next April, the official staff of the Association is busily engaged in planning constructively for the successful culmination of the present year's work. One important step in that direction of interest to all members of the Association is a meeting to be held next month.

On Sunday, December 14, at the Orange Court Hotel in Orlando, the Committee on Scientific Assembly and Specialty Group Problem will meet to confer upon the advisability of altering the present plan of Scientific Assemblies and Specialty Group Meetings at the annual conventions of the Association. An open forum will afford all members the opportunity of expressing their views on this vital matter. They are urged to give the Committee the benefit of their suggestions and considered judgment at this meeting so that its report to the House of Delegates may reflect as fully as possible the wishes of the entire membership.

In accordance with a resolution presented by the Orange County Medical Society and adopted by the House of Delegates at the 1952 Annual Meeting, as Chairman of the Board of Governors I appointed this Committee. Its membership consists of Dr. Herbert E. White of St. Augustine, Chairman, and Drs. Jere W. Annis of Lakeland, Reuben B. Chrisman, Jr., of Miami, Frederick K. Herpel of West Palm Beach, Louis M. Orr, II, of Orlando, R. Wynn S. Owen of St. Petersburg, James N. Patterson of Tampa, Shaler Richardson of Jacksonville, and William C. Roberts of Panama City. Dr. White, the Chairman, will communicate with the members of the Association about the meeting.

The resolution points out that most specialty societies hold their annual meetings on the weekend immediately preceding the Annual Meeting of the Association. Many of their members leave on the first day of the Association's meeting, and it is contended that the attendance upon the scientific sessions is affected. Since the scientific sessions should be set up for the greatest benefit of all the members, the resolution seeks careful evaluation of the problem by this Committee with the cooperation of the entire membership.

Not alone the presidents and secretaries of all county medical societies and of all specialty groups, but each and every member of the Association is urged to give thoughtful consideration to this matter and then voice his opinion to the Committee at the Orlando meeting scheduled for 11 a.m. on December 14. What do you think about it, Doctor?



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## Taking Stock

In the midst of spacious grounds, there stands in a small mid-Western city a stately mansion of early nineteenth century vintage. It serves that thriving manufacturing center today as the City Hall, and all who come and go are reminded that the doughty New England pioneer who sought and won his fortune in that Western outpost of his day was aware that he succeeded not in his own strength alone. Beautifully carved on the mantel of the fireplace in the great hall are these words, "God's providence is mine inheritance." He did not fail to give thanks to the Source of his blessings.

In this month of football extravaganzas and turkey dinners, America traditionally pauses to observe Thanksgiving Day. Formally, by presidential proclamation, she acknowledges her manifold blessings. Every individual citizen likewise would do well to take stock of the bounty that is his in this land of, as yet, freedom and abundance. Before partaking of his Thanksgiving feast, every American might appropriately emulate the Founding Fathers of this great nation by placing first upon his empty plate five grains of corn, symbolic of the struggle for survival of the Pilgrims in their quest for freedom.

God's providence has indeed been the heritage of this nation, called today into a position of world leadership. Let America not squander this heritage. Rather, because of it, may she ward off external threats and insidious onslaught from within. May she draw back in time from the yawning abyss of entangling alliances and foreign ideologies which threaten disaster in these days of unprecedented peril. Let her continue to chart her course in the strength of the beneficent Providence which has made her strong and thereby measure up fully to the large place into which she has been called.

The medical profession also may well count its blessings at this appropriate season. In this healthiest of nations, the average life span has increased 20 years in the last half century. The level of medical education here is unsurpassed anywhere in the world, as are standards set for hospital and medical care. Medical research has made remarkable progress, and the battle against many diseases has been or is being won. The encroachment of government in medicine constitutes the one outstanding sinister note. As we give thanks for the achievements to which we may point with pardonable professional pride, let us gird ourselves for teamwork in fighting the battles that lie ahead, secure in the providential guidance which is our heritage. Let us ever be mindful that a charge to keep we have.

## Important Court Decision in Hoxsey Cancer Case

Of wide interest to physicians is the opinion of the United States Court of Appeals for the Fifth Circuit in the case of U. S. v. Hoxsey Cancer Clinic, a Partnership, and Harry M. Hoxsey, an Individual, which was handed down at New Orleans recently. This opinion resulted from an appeal in a vigorously contested case tried in the United States District Court at Dallas, Texas, and reverses the judgment of the lower trial court judge. It directs that Court to issue an injunction prohibiting the defendants from distributing in interstate commerce brownish-black, and pink, liquids intended for the treatment of cancer in man.

The Hoxsey Cancer Clinic, opened in 1936, is located in Dallas and ships its products to patients in practically every state in the country. Its "Medical Director," an osteopath named Dr. Joseph Durkee, testified that during his association with it during the past five or six years, he personally had examined and treated five or six thousand patients, at the rate of 35 to 50 a day. At the time of the trial the fee was $400 per patient.

Many physicians across the nation are being asked about the Hoxsey medicines, one of which is for internal and the other for external treatment. That for external use, reports the Division of Medicine of the Food and Drug Administration of the Federal Security Agency, is composed of several escharotics and was not an issue in the trial. Of the two medicines for internal use, the black or brown medicine contains cascara sagrada, potassium iodide, extracts of buckthorn, prickly ash, red clover blossom, alfalfa, sugar and water; the pink liquid is chiefly elixir of lactated pepsin containing variable amounts of potassium iodide. "Supportive treatment" consists of preparations containing iron, urinary antiseptics, vitamins, laxatives and antacids.

The unanimous opinion of the Court of Appeals was that "the overwhelming weight of the credible evidence requires a conclusion that the representation that the Hoxsey liquid medicines are efficacious in the cure of cancer is*** false and misleading. The evidence as a whole does not support the finding of the trial Court that 'some it cures, and some it does not cure, and some it relieves somewhat.'" In addition to distinguished medical specialists, more than 50 physicians from throughout the country gave of their time to testify for the government, enabling it to present scientific evidence that Hoxsey's claimed "cures" were allegedly effected in (1) patients who had never had cancer and were treated at the Hoxsey Clinic for it, (2) those cured of cancer before being treated for it there, and (3) those who had cancer and still have it or who died under the Hoxsey treatment.

In a letter with enclosures to State Health Officers, C. W. Crawford, Commissioner of Food and Drugs, presented the foregoing information and enumerated the important principles laid down in the Circuit Court opinion, based on testimony by cancer experts. These principles are:

1. "*** there is only one reliable and accurate means of determining whether what is thought to be cancer is, in truth and fact, actually cancer. This requires a biopsy, a microscopic examination of a piece of tissue removed from the infected and diseased region."
2. "***the opinion of a layman as to whether he has, or had, cancer, or a like opinion as to whether he has been cured and no longer bears the disease, if, in fact, it ever actually existed, is entitled to little, if any, weight."
3. "***despite the vast and continuous research which has been conducted into the cause of, and possible cure for, cancer the aggregate of medical experience and qualified experts recognize in the treatment of internal cancer only the methods of surgery, X-ray, radium and some of the radioactive by-products of atomic bomb production."
4. "***Upon such subjects a Court should not be so blind and deaf as to fail to see, hear and understand the import and effect of such matters of general public knowledge and acceptance, especially where they are established by the overwhelming weight of disinterested testimony***."

This Court of Appeals decision greatly strengthens the hand of the government in its fight against worthless cancer treatment. Under the law, however, the defendants still have the right to petition for review by the United States Supreme Court.

## Electric Vaporizing Devices for Insecticides Present Health Hazards

Several types of generators of insecticide vapors or fumes are now advertised or proposed for use in homes, food establishments, industrial plants, hospitals and schools. The devices commercially available include automatic, thermostatically controlled and manually controlled electric vaporizers which operate continuously, unless the light bulb or heating element serving as the source of heat is turned off. Growing general concern over the efficacy and safety of these electric vaporizing units for the dispersion of insecticides within buildings prompted a recent evaluation of the available data by the Committee on Pesticides of the Council on Pharmacy and Chemistry of the American Medical Association.[1]

In the report of this committee it is explained that the electrically operated thermal generators employ technical DDT, lindane, or a mixture of the two in an inert base with a composition which may include substances such as glycols, carbowaxes, bentonite, or other clays. From a cup in the generator the insecticidal ingredients are evaporated by a built-in heating element or some other heat source, such as an electric light bulb. For the automatic, thermostatically controlled apparatus, the recommended rate of discharge is 1 Gm. of insecticide in 15,000 cu. ft. for a 24 hour period. Under comparable conditions, greater concentrations may be expected with the more inadequately controlled, manually operated machines.

Discharged as vapors or fumes, these ingredients ultimately recrystallize on the ceiling, walls, and other exposed surfaces in varying amount and surface distribution pattern. Loose crystals may even become dislodged and fall to the floor or other horizontal surfaces below, a tendency greatest with devices employing DDT. The atmospheric dispersal of the vapors or fumes is likewise irregular. It is estimated that "if the average active person breathes approximately 10 cu. m. of air in an eight hour period, the maximum theoretical intake of insecticide may be approximately 1.3 to 13 mg. of DDT or 0.9 to 2 mg. of lindane during a normal work-day period." The DDT level in the atmosphere ("0.13 to 1.3 mg. [0.009 to 0.09 ppm] per cu. m. of air when dispensed by a properly operating, thermostatically controlled machine") approaches a concentration which might be considered to exceed a safe level for continuous exposure over a prolonged period of time. The lindane concentration ("0.09 to 0.2 mg. [0.008 to 0.017 ppm] per cu. m. of air") is below the estimated safe level, although regular and continuous exposure is considered unwise.

Taking cognizance of the health problems associated with the use of these devices, the Interdepartmental Committee on Pest Control, composed of representatives of the Departments of Agriculture, Interior, and Defense and the Federal Security Agency, issued a statement recently on the health hazards of the automatic "vaporizer." It recommended use of such devices employing DDT, BHC (benzene hexachloride), or mixtures of the two only where human exposure is on a normal working day basis, as in commercial establishments, and at a rate not to exceed 1 Gm. to 15,000 cu. ft. for a 24 hour period. Other recommendations included caution against continuous exposure to the devices and against their use in homes and sleeping quarters.

Since this statement was issued, the Committee on Pesticides of the Council has received a number of reports of poisoning. Urticaria, mild peripheral neuritis, severe headache, nausea and irritation of the eyes, nose and throat have been reported in employees of food-dispensing establishments, industrial workers and others.

Limited federal regulatory power has led several states and municipalities to recognize the urgency of this problem at the state and local level and to consider ordinances and other types of appropriate regulations.

1. Health Hazards of Electric Vaporizing Devices for Insecticides, J. A. M. A. 149:367-369 (May 24) 1952.

## The Case of Patient Versus Case

Is the case admitted to the hospital, or is the patient? Does the case have a fever, or does the patient? Is the case operated on, or is the patient? Ask the patient, and he is apt to vote for himself. Ask the doctor, and he may take a less personal, even less accurate view.

A case is a particular instance of disease, the totality of the symptoms and of the pathologic and other conditions. A patient, on the other hand, is the human being afflicted. Much medical literature to the contrary notwithstanding, proper medical writing restricts the use of the word case to the broad concept of an instance or example of disease, the totality of what is known about the patient, his condition and all the circumstances. One medical dictionary (Dorland's) takes the trouble to add to the definition of case that "a

case is not synonymous with a patient, for the latter is the human being affected with the disease." Moreover, the patient and his condition are the concrete subjects with which one deals, and referring to them specifically rather than to the abstract term case will simplify and vivify writing.

Too, care in this particular may serve as a reminder that, after all, patients are persons, not an assembly of symptoms. It has been pointed out that a major difficulty with modern medical education is "a tendency to teach that man can be understood exclusively through an unfolding of his inherited biological endowment in a given physical setting." A recent report[1] of the American Psychiatric Association points out that "this viewpoint fails to take into account human personality and the influence of interpersonal and cultural factors on personality development and physiological functions."

The pendulum, however, now tends to swing in the right direction, so that physicians of the future will peer right through the laboratory reports and the clinical charts to see the patient himself in the light of his feelings, his fears and his personal problems as well as his aches and pains. In leading medical schools today, the undergraduate medical student studies the principles of psychiatry. Commending this training as evidence of a correct trend, the report indicates that he needs to have a much broader concept of human biology in order to use his training effectively in dealing with patients as persons.

It appears that in the future the case of patient versus case will tend more and more to be decided in favor of the patient.

1. Treat Patients as Persons, Science News Latter 61:395 (June 21) 1952.

## A. M. A. Coordinating Committee Disbands Whitaker and Baxter Resign

Its primary objective attained, that of warning the American public of the evils of compulsory health insurance and making known the advantages of the American way of voluntary health insurance, the Coordinating Committee of the American Medical Association was recently dissolved by an action of the Board of Trustees. This Committee has been supervising the National Education Campaign for the past four years. Dr. Elmer L. Henderson of Louisville, past president of A. M. A., has served as chairman since its inception.

The west coast public relations firm of Whitaker and Baxter, which has been doing an outstanding job of directing the National Education Campaign, has resigned and no longer has any official connection with the A. M. A. American physicians, in fact citizens in every walk of life, owe an everlasting debt of gratitude for the effective, efficient and courageous campaign this firm waged in the face of formidable opposition.

Whitaker and Baxter have accepted the assignment of directing the National Professional Committee for Eisenhower and Nixon. This new professional committee will seek to enlist physicians, dentists, lawyers, engineers, pharmacists, accountants and other professional men and women in an aggressive, bipartisan drive for the election of the Republican nominees for president and vice president. Dr. Henderson will serve as chairman of this new committee. He will be aided by A. M. A. past presidents Drs. Ernest E. Irons, Chicago, and John W. Cline, San Francisco, in the capacty of vice chairmen.

Other vice chairmen, who are also past presidents of their respective national professional associations, include: Harold J. Gallagher, New York, American Bar Association; Dr. Clyde E. Minges, Rocky Mount, N. C., American Dental Association; Robert Lincoln McNeil, Philadelphia, American Pharmaceutical Manufacturers' Association; Sidney L. Stolte, St. Paul, National Society of Professional Engineers; and John F. Forbes, San Francisco, American Institute of Accountants.

Both Dr. Henderson and Whitaker and Baxter severed their official connections with A. M. A. in order that they may individually assist in campaigns for candidates for federal elective offices. Such action is entirely within the rights and privileges of every American citizen.

The A. M. A. as a non-partisan professional organization is barred, both ethically and legally, from participating in national election campaigns. These laws and principles apply equally to F. M. A. and county medical societies. It is a violation of the F. M. A. policies to engage in political activities on any level. Precedence set in the early days of the Association and conscientiously followed down through the years, presumes adherence to this principle.

It is the lawful and bounden duty of medical societies on local, state and national levels to study and analyze medical laws and proposed legislation which will affect the health of the people. Legislators frequently consult medical societies and hometown doctors for advice on matters of

this kind. It is essential that the A. M. A., the F. M. A. and county medical societies keep their members informed so that they will be able to give sound counsel. It equally holds that each member owes it to his country and his profession to study the information assembled and disseminated by his professional organizations to aid him in making decisions.

Doctors may engage in political activities as individuals. However, they have no right, nor any authority, to use the name of the A. M. A., the F. M. A., or their county medical society in this connection. Officers of professional organizations must exercise particular caution that their statements and actions cannot be construed as endorsements by the organizations which they represent.

### Well Done, Whitaker and Baxter

It is with deep regret that we say farewell to Whitaker and Baxter as they sever official connections with the A. M. A. The Journal salutes them for a difficult task superbly executed.

Brought into the medical family nearly four years ago to direct the newly conceived National Education Campaign, these two dynamic personalities gave freely of their time and talents in presenting to the American public a story sadly in need of telling. Clem Whitaker and Leone Baxter portrayed the evils of government controlled medicine so effectively that today there is a positive trend, not only toward health insurance the voluntary way, but refreshingly away from socialistic doctrines of all kinds. They, together with the rank and file of American physicians, have sparked a desire to restore this country to sound democratic principles of local autonomy and individual freedom.

We have every confidence that these public relations experts will be eminently successful, whatever their assignment. Our best wishes go with them.

**FORTY-SIXTH ANNUAL MEETING**
**SOUTHERN MEDICAL ASSOCIATION**
**MIAMI**
**NOV. 10-13, 1952**

### A.M.A. Clinical Session Denver, December 2-5

In Denver's newly enlarged Municipal Auditorium, the American Medical Association will open its sixth annual Clinical Session on Tuesday morning, Dec. 2, 1952, with the scientific exhibit, medical motion pictures, the technical exposition and registration. On Tuesday afternoon colored television will be shown, with general lectures in the main auditorium, followed by clinical presentations in eight meeting rooms adjacent to the technical and scientific exhibits. Geared to the general practitioner, the meeting will feature practical demonstrations on various phases of medicine of special value to him.

The scientific exhibit, consisting of some 60 exhibits, will cover a wide range of medical subjects and will provide the general practitioner with a postgraduate course in such subjects as office anesthesia, cardiology, dermatology, endocrinology, gynecology, laboratory procedures, otolaryngology, pediatrics and proctology. Emphasis will be on diagnosis and treatment. At stated times, mannikin demonstrations will be given on the problems of delivery. One exhibit will cover fractures of the spine, wrist and ankle. Demonstrations on artificial respiration will use the new back-pressure arm-lift method.

Clinical presentations during the four day session include nearly 200 lectures on obstetrics, pediatrics, diseases of the chest, cardiovascular diseases, neurology and psychiatry, fluid balance and renal problems, traumatic surgery, and medical therapy. In addition, eminent guest speakers from various sections of the country will lecture on hypertension, bone tumors, urinary infections in children, methods of parenteral protein feeding, and other basic subjects.

Colored television, originating from Denver General Hospital, will bring the operating room directly into the convention hall.

The technical exposition on the arena floor will be conveniently located adjacent to the registration desks and two of the meeting rooms.

Physicians may plan to attend a full day of activities without leaving the auditorium for restaurant facilities will be available in the building. There will be a diversified entertainment program each evening.

On Monday, December 1, the day preceding the opening of the Clinical Session, the annual Medical Public Relations Conference will be held.

## FLORIDA BLUE SHIELD

### A Message To Blue Shield Physicians

The first Medical Society-Blue Shield Liaison Committee meeting to be held since the organization of the committees throughout the State took place in Miami on August 27, 1952, and was a joint meeting of the Dade and Broward County committees. Blue Shield president Dr. Leigh F. Robinson's message to the joint gathering so well described the background and purposes of Blue Shield and its close affiliation with the medical profession that his message is reprinted for the benefit of all physicians.

"I believe that the county committees appointed by the medical societies are an important step toward maintaining the understanding between participating physicians and the Blue Shield Plan. Every medical society has members who have not had the opportunity to become familiar with Blue Shield. It is particularly for this group of physicians that the county Blue Shield committees can be most helpful whenever questions are asked regarding the why and wherefore of Blue Shield.

"Many laymen and some physicians, because of lack of knowledge, labor under the impression that the medical profession sponsored Blue Shield for the purpose of insuring payment of their bills. Nothing could be further from the truth. On the contrary, the members of the medical profession became interested in voluntary health insurance because they became very frightened in the 30's and 40's that the Washington government was going to be successful in passing a compulsory type of health insurance. Congressmen and Senators over the United States who were unfavorable to socialization of medicine told their doctor friends back home that opposition in Congress to compulsory health insurance was doomed to crumble unless something could be offered in its place. The doctors were told by their friends in Congress who were close to the pulse of the people that a voluntary type of prepayment health insurance would be preferred by the American public, and although commercial companies were offering group health plans they offered too little to meet the arguments of the proponents of governmental compulsory health insurance. Surveys of group employers and employees indicated that the average man in the low income bracket wanted a package type of coverage which would protect him against catastrophic conditions which required hospitalization. These employer groups indicated that they desired a medical plan for meeting medical bills similar to that which was being offered by the Blue Cross for the prepayment of hospital bills. These groups further indicated that such a coverage must guarantee to the low income worker, (1) full payment of all surgical bills requiring hospitalization, and, if possible, maternity bills, (2) a low premium rate, and (3) guarantee that the medical profession woud agree to render the services offered by the Plan.

"It was in the middle 30's when these arguments were being spread by both the lay and medical press throughout the country. The American Medical Association was being criticized by the profession for not initiating a medical care plan as the American Hospital Association had done in sponsoring Blue Cross. The doctors throughout the country became so impatient with the apparent delay of the American Medical Association that they began organizing small surgical plans on county and state medical society levels. Almost immediately these groups of physicians were astonished by the popularity and success of their Plans. The favorable comment of both the lay and medical press and the growing demand of large groups of employees and employers for this new type of health coverage stimulated state medical societies all over the United States to sponsor for their areas similar health plans. The movement once underway progressed far beyond their fondest hopes and expectations. Today, there are very few communities in the United States and Canada that are not served by these health plans, now known as Blue Shield Plans.

"In the beginning the only experience and actuarial tables were those possessed by commercial companies offering surgical and maternity coverage which, as shown above, were employed by the Blue Shield Plans. As the movement has expanded some of the larger Plans whose reserves permitted experimentation have been offering additional medical benefits. Our own Plan, acting upon the experience of larger Plans, has added during the past two years some medical benefits. At the present time a committee is making a survey of all benefits, especially medical benefits, of commercial and Blue Shield Plans throughout the United States and Canada in order to learn whether or not it will be feasible for Florida Blue Shield to increase its medical and other services. It should be emphasized that this desire of the Florida Blue

Shield to add other types of benefits for the subscriber is only for the purpose of increasing the value of the policy to the subscriber. In other words, the policy of your Blue Shield is, and must always be, to give the subscriber first and last consideration in the expenditure of the subscriber's money. This means that any increase of benefits of Blue Shield must be for the subscriber and not necessarily for the doctor. This at first may seem illogical because it would appear that any increase of benefits to the subscriber would benefit the doctor, or on the other hand, any increase of fees for the doctor would also benefit the subscriber. This is not always true, because an increase of fees to the physician could weaken and make insolvent the Plan. The doctor should, and in most cases does, feel that he is well remunerated because he is a link in the chain that has stymied to date all governmental efforts to impose socialized medicine on the public.

"In closing, I want to express my appreciation to each and every one of you for accepting an appointment on your County Medical Society Blue Shield Committee and to assure you that the directors, officers and the executive director are always at your command."

## BIRTHS AND DEATHS

### Births

Dr. and Mrs. James J. Hutson of Miami announce the birth of a son, Micah Graham, on May 8, 1952.

Dr. and Mrs. S. Roy Higginbotham, Jr., of Tampa announce the birth of a daughter, Kathleen Lynn, on Aug. 21, 1952.

Dr. and Mrs. Theodore J. Grable of Tampa announce the birth of a son, William DeTar, on Aug. 22, 1952.

Dr. and Mrs. William W. Trice of Tampa announce the birth of a son.

### Deaths — Other Doctors

McKey, Earle S., Jr., Valdosta, Ga.....April 28, 1952

## NEW MEMBERS

The following doctors have joined the State Association through their respective county medical societies.

Britt, Otis W., Tallahassee
Davis, H. Clinton, Miami
Harris, Tyndall P., Jacksonville
McCallister, Archie, Jr., Miami
McShane, James K., Jr., Miami
Ramey, John R., Miami
Saxon, Roy F., Jr., Tampa
Wolkowsky, Melvin, Miami Beach
Zipser, Lester L., Tampa

## STATE NEWS ITEMS

Dr. Herbert E. White, St. Augustine, chairman of the Committee on Scientific Assembly and Specialty Group Problem, has called a meeting open to all members of the Association at 11 a.m. on Sunday, Dec. 14, 1952, at the Orange Court Hotel, Orlando. The purpose of this meeting is to consider the advisability of rearranging the set-up on scientific assemblies and specialty group meetings at the Association's annual meeting. Every member interested in this problem is urged to attend the meeting.

Consideration of this problem is a result of an action by the House of Delegates at Hollywood in April 1952 when it approved a resolution introduced by the Orange County Medical Society, "That the Board of Governors appoint a committee to consider this problem during the coming year and report to the 1953 session of the Florida House of Delegates."

Following the close of the open forum for all members of the Association, the Committee will retire to prepare a report for presentation at the 1953 meeting of the House of Delegates.

In addition to Dr. White, President McIver has appointed the following members on this Committee: Drs. Jere W. Annis, Reuben B. Chrisman, Jr., Frederick K. Herpel, Louis M. Orr, II, R. Wynn S. Owen, James N. Patterson, Shaler Richardson and William C. Roberts.

The many friends of Dr. Joseph S. Stewart, Miami, will be pleased to learn that his presidential address presented during the Atlanta Assembly of The Southeastern Surgical Congress, Atlanta, March 10-13, 1952, has been published in the June 1952 issue of the American Surgeon.

In his inimitable style, Dr. Stewart has reviewed our rich American heritage with particular emphasis upon the part the South has contributed to that heritage. The wisdom written into the Constitution by its framers is portrayed. In conclusion the medical profession is advised of its responsibility, along with other dutiful citizens, to work diligently and constantly in order to protect this heritage and preserve the Constitution from the inroads of socialistic doctrines.

Dr. Thos. S. Griggs, formerly of Miami Shores, has started the second year of his residency in anesthesia at Charity Hospital, New Orleans.

Upon invitation from the Southern Medical Association, the F. M. A. Committee on Public Relations will have a booth at the annual meeting, November 10-13, in Miami, to show some of the highlights of the Association's public relations program. Dr. Eugene B. Maxwell, Tampa, chairman of the Committee on Public Relations, has arranged for the exhibit which will be manned by personnel from the Bureau of Public Relations.

Dr. John M. Schultz, 2300 Biscayne Boulevard, Miami, recently returned from New York City after an extended leave of absence, taking special work in different forms of therapy for gynecolgical center, etc. Dr. Schultz will limit his practice to sterility and Gynecology.

The Florida Obstetric and Gynecologic Society will hold its Third Annual Mid-Winter Scientific meeting at the Soreno Hotel in St. Petersburg, Saturday afternoon and Sunday morning, December 6 and 7. The guest speaker will be Dr. John Nokes, Associate Professor of Obstetrics and Gynecology, the University of Virginia Department of Medicine.

Dr. Rene A. Torrado of Miami Beach spoke on cancer over radio station WMBM recently. He was guest speaker on the Hungarian-American Culture Club program.

Appearing on the WTVJ television program "Modern Living" in September were Drs. Joseph J. Groom of Miami who spoke on "Cataracts;" Harold Rand of Miami who spoke on "Emotions and Allergies;" Howard A. Engle of Miami Beach who spoke on "Cerebral Palsy;" and Carl M. Midkiff of Miami Shores who spoke on "Food Poisoning."

Dr. Frank G. Slaughter of Jacksonville spoke on "Disease and Destiny" at a recent meeting of the Mandarin Community Club.

Dr. Edward R. Annis of Miami recently addressed the Miami Acacia Club on "Let's Live a Little Longer."

Dr. J. M. Ingram, Jr., of Tampa has been named chairman of the executive committee of the Hillsborough County Unit of the American Cancer Society. He succeeds Dr. C. Frank Chunn of Tampa who has resigned from active service on the committee after serving as its chairman since its organization three years ago.

A new portable exhibit designed for lay audiences and entitled, "Health — 1952" is available from the A. M. A.'s Bureau of Exhibits for state and county medical societies. The exhibit presents an over-all picture of health conditions in the United States at the present time. The Bureau plans to revise and bring the exhibit up to date each year. The only cost involved to medical societies will be the shipping charges both ways.

Dr. Lorenzo L. Parks of Jacksonville, Commander of the 202nd Medical Battalion of the Florida National Guard, announces that any physician who is interested in devoting a small amount of time to the Florida National Guard may do so by contacting one of the Florida National Guard Units in his home town or near by for information. As this Journal goes to press, physicians in Priority 3 may become members of the National Guard and then they are not subject to the draft. Physicians not living in a town where there is a National Guard Unit may be assigned appropriate duty and make drills in neighboring towns.

Drs. Hawley H. Seiler, Tampa, and DeWitt C. Daughtry and John G. Chesney of Miami were among the speakers at the Thirty-Ninth Annual Southern Tuberculosis Conference at the Roney Plaza Hotel in Miami Beach recently.

Dr. Franklin J. Evans of Coral Gables recently spoke on the WTVJ "Law of the Land" program.

Dr. George F. Schmitt, Jr., of Miami spoke at a recent meeting of the South Miami Lion's Club. His subject was "The Wellspring of Your Existence."

Drs. Clarence Bernstein and Solomon D. Klotz of Orlando recently presented a special report to the Annals of Allergy, which appears in the July-August issue of that journal. The study covered four years of work with a new antihistamine drug.

Dr. Valpeau H. Ragsdale of Pierce was recently honored for long and faithful service by the communities within a 15-mile radius of Pierce. The program included a picnic, speech-making and entertainment, and was held at the Pierce Community Center.

**46th Annual Meeting**
**SOUTHERN MEDICAL ASSOCIATION**
**Miami, November 10-13**

A most cordial welcome awaits physicians of the South attending the Miami meeting of the Southern Medical Association. The meeting will consist of forty-nine half-day sessions presented by the twenty-one sections of the Association, which embrace every phase of medical practice. In addition to the section sessions there will be a general session, the annual dinner of the Association and outstanding scientific and technical exhibits.

This meeting will be the opportunity of the year for physicians of the South to attend a complete general medical meeting and at the same time enjoy a much-needed vacation during one of the most delightful periods of the year in beautiful Miami.

All activities of this meeting will be in the Municipal Auditorium in Bayfront Park and in near-by hotels, everything within walking distance. Good hotel accommodations are available for all who wish to attend this outstanding medical meeting.

**Regardless of what any physician may be interested in, regardless of how general or how limited his interest, there will be at Miami a program to challenge that interest and make it worthwhile for him to attend.**

Members of state and county medical societies may attend. Eligible physicians, members of state and county medical societies in the South **can be** and **should be** members of the Southern Medical Association. The annual dues of $10.00 include the Southern Medical Journal, a journal most valuable to physicians of the South, one that each should have on his reading table.

**SOUTHERN MEDICAL ASSOCIATION**
**Empire Building**
**Birmingham 3, Alabama**

Dr. Eugene B. Maxwell of Tampa, chairman of the Association's Committee on Public Relations, met with a group of Tallahassee physicians October 8 in Tallahassee to discuss preparations for showing the Association's Fair Exhibit at the North Florida Fair, October 27-November 1. Tom Jarvis, assistant supervisor of the Association's Bureau of Public Relations, also attended the meeting.

Dr. Joseph H. Lucinian of Miami has returned to his practice after attending a meeting on roentgenology in Houston, Tex.

Dr. James T. Cook, Jr., of Marianna presided recently at the first meeting of the executive board of the local P.-T.A. Dr. Cook is president of the board.

Dr. Meyer Yanowitz of Miami spoke on "Common Aids in Dermatologic Practice," at a recent meeting of the Miami chapter of the Florida Society of Medical Technologists.

Dr. Shaler Richardson, Jacksonville, chairman of the Medical Advisory Committee to the Florida Council for the Blind, and Drs. Charles C. Grace, St. Augustine; Sherman B. Forbes, Tampa; Bascom H. Palmer, Miami, and Nathan S. Rubin, Pensacola, members of the Committee, met with the Boardmen of the Council in Daytona Beach recently.

The Association's display, "My Doctor," was shown at the annual conference of county and home demonstration agents from all over the state, October 5-10, in Gainesville. A series of six illustrations based on the physician's requirements as set forth in the A. M. A.'s Principles of Medical Ethics, the display originally was used during the recent Farm and Home Institute meetings at Camp Timpoochee, near Niceville, and Camp Cherry Lake, near Madison. The showing at Gainesville was part of the Association's Rural Educational Program.

Dr. Robert B. McIver of Jacksonville, as president of the Jacksonville Blood Bank, accepted on behalf of the Blood Bank, a certificate of achievement for having collected 10,719 pints of blood for the Armed Forces Blood Program on October 8.

Dr. Frank E. Wilson, Director; Mr. James Foristel, attorney of the A. M. A. Washington office; and Dr. Julian Price, Florence, S. C., a member of the A. M. A. Committee on Legislation, met in Jacksonville on October 15 with key members of the Florida and Georgia state medical associations and their woman's auxiliaries.

The primary objective of the meeting was to acquaint the medical leaders of the two states with the latest information on the national legislative picture. This Florida-Georgia meeting is one of a series being conducted throughout the United States by representatives from the A. M. A. Washington office.

Dr. Carlos P. Lamar of Miami, representing the Dade County Medical Association, spoke at a public meeting sponsored jointly by the "Alianza Interamericana" and the "Mental Health Society of South Florida" on September 7. Following the showing of the film, "City Hospital," Dr. Lamar spoke on "Psychosomatic Medicine" and discussed the film.

Dr. W. Wardlaw Jones of Dade City spoke to the Dade City Rotary Club at a recent luncheon meeting. His subject was the county hospital and its needs.

Dr. David R. Murphey, Jr., of Tampa has been appointed chairman of the local medical and nursing subcommittee for the 1952-53 Red Cross disaster organization.

## WANTED — FOR SALE

**Advertising rates for this column are $5.00 per insertion for ads of 25 words or less. Add 20c for each additional word.**

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## COMPONENT SOCIETY NOTES

### Dade

At the regular October meeting of the Dade County Medical Association, a symposium on pediatric cardiology was held. Participating were Drs. Herbert Eichert who spoke on "Facilities Available in Dade County," Milton S. Saslaw who spoke on "Rheumatic Heart Disease in Miami (Studies and Views)," Francisco A. Hernandez who spoke on "Cardiac Catheterization (Method and Value)," and Jack L. Wright who spoke on "Activities of a Diagnostic Service."

### DeSoto-Hardee-Highlands-Glades

At the regular September meeting of the DeSoto-Hardee-Highlands-Glades County Medical Society, which was held at Aqua Vitae Springs, Zolfo, guest speakers were Drs. Wesley W. Wilson and Leffie M. Carlton, Jr., both of Tampa. Dr. Wilson spoke on "Skin Tumors About the Eyelids," and Dr. Carlton spoke on "Cancer of the Lung."

### Duval

At the regular meeting of the Duval County Medical Society in October, Dr. Jack Mickley, medico-legal expert of Harvard University, spoke on the legal problems that might be encountered by a physician in his practice.

### Hillsborough

At the regular meeting of the Hillsborough County Medical Association on October 7, Dr. J. M. Ingram, Jr., spoke on "Occult Rupture of the Uterus."

### Lake

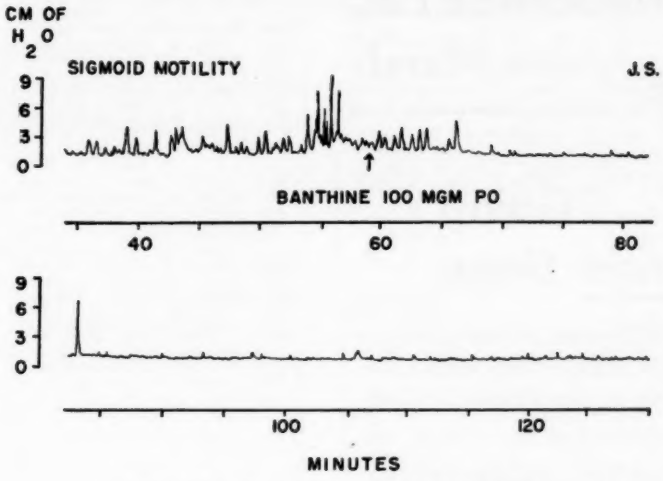
At the September meeting of the Lake County Medical Society, Dr. Robert W. Young of Orlando spoke on "Arthritis."

### Marion

At the regular September meeting of the Marion County Medical Society, Dr. Chester A. Fort, assistant urologist, Emory Medical College, Atlanta, spoke on "The Present Indications for Uretero-Intestinal Anastomosis."

### Monroe

At a recent joint meeting of the Monroe County Medical Society and the staff of the United States Naval Hospital in Key West, Drs. John Elliott and Donald W. Smith, of Miami, spoke on research and clinical work in shock condition. Dr. Smith also read a paper on "Nitrogen Balance in Critically Ill Patients."

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1. Kern, F., Jr.; Almy, T. P., and Stolk, N. J.: Effects of Certain Antispasmodic Drugs on the Intact Human Colon, with Special Reference to Banthine (β-Diethylaminoethyl Xanthene-9-Carboxylate Methobromide), Am. J. Med. *11*:67 (July) 1951.

2. Lepore, M. J.; Golden, R., and Flood, C. A.: Oral Banthine, an Effective Depressor of Gastrointestinal Motility, Gastroenterology *17*:551 (April) 1951.

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From where I sit *by* Joe Marsh

## Going . . . Going . . . Almost Gone

Granny Robinson put on quite a show the other night at the White Elephant auction at the Women's Club.

*Towards the end of the evening, she had the ladies really battling for anything she put up. "What am I bid for this woman's lovely black coat here—good as new? Who'll say ten dollars?" she asked.*

Granny held the coat up, and commenced describing the lining, sleeves, buttons—really "selling hard." Then, suddenly, she took a *close* look and blurted out "Land sakes, no more bidding—this is *my own* coat!"

*From where I sit, what almost happened to Granny was good for a laugh, but sometimes when people "get carried away" with their own talk it's not so funny. Like those who would tell others how to practice their profession . . . like those who would interfere with my right to a temperate glass of beer. I suggest we hold on to our opinions—and believe in them—but take a close look at them before we try to "sell" them to our neighbor!*

Joe Marsh

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### The Time Has Come

The A. M. A. National Education Campaign is officialy ended by action of the Board of Trustees. Four vital, constructive years were spent in this educational endeavor by members of the medical profession and their lay representatives.

It was an historic undertaking. In its great crusade against socialization, it stood like a beacon of liberty with arm uplifted pointing the way out of legislative meshes which were being knit about the body medicine.

This activity made a landmark in the history of American medicine. It meant the difference between life and suffocation of the profession and preservation of the principles in which it believes. It was effective because of combined efforts of millions of individuals from every group, who stood united in resistance to a compulsory system which threatened the freedom and safety of the nation's health under the misleading nomer of insurance.

The results of this educational campaign became evident in the accelerated growth of voluntary health insurance plans which evinced the healthy vigor of a people who prefer to choose a method of self-protection rather than wear the yoke of a compulsory measure.

Dr. Elmer L. Henderson, chairman of the American Medical Association's Coordinating

Committee, which has supervised the campaign against socialized medicine, has resigned his committee chairmanship so that he may be free to participate in the presidential election campaign. Clem Whitaker and Leone Baxter, Directors of the A. M. A. National Education Campaign, have asked to be released from their duties for the same reason.

For, it must be remembered, the A. M. A. is a nonpartisan, professional organization and is barred both ethically and legally from participating in election campaigns. Dr. Henderson and Whitaker and Baxter, in asking for their release from A. M. A. duties, do so in order that they may be free to participate in the campaign. This is the right of every individual.

Neither the A. M. A. nor the F. M. A. will take part in the presidential election except to join with other nonpartisan groups in urging all eligible voters to cast their ballots on election day regardless of their affiliations or preference. However, a doctor and his wife are entirely free to participate in election activities as individuals. In fact there is a real responsibility to make their influence felt in the interest of good government.

For, in having wrestled with socialism and discouraged it at the gates of medicine, we can be sure this ideology will creep in another entrance and like in the fable of Beowulf who did battle with Grendel, we see depicted a monster whose appetite was fed on the vigour of the nation's vitality — its independence. Its approach was concealed under a fog, its method was to lull to sleep; placing a spell upon those who slept to make them sleep more soundly. The responsibility falls to the Beowulfs of every age who by effort manage to see what manner of thing this socialistic Grendel is.

The legends of old are timeless because they immortalize the constant struggle between good and evil and the obligation of man is summed up in the words of Hygelac: "The time has come, O Beowulf, for you to prove your worth. The Gods have gifted you with the strength of thirty men, and this strength you should use to the advantage of your fellows. . . . Our neighbor is in sore need. Go forth and do mortal combat with this Grendel-fiend."

Mrs. C. Robert DeArmas


## *Migraine In Children*

**"Migraine may appear during the first years of life. The presence of subjective signs, such as headache and flimmer scotoma, is often difficult to determine in young children. The true nature of the symptoms frequently remains obscure for years."**

Vahlquist, B. and Hackzell, G.: Acta Paediatrica *38*: 622 (1949).

| NO. OF CASES | SEX | AGE AT ONSET | CYCLIC VOMITING | DURATION OF ATTACK | INTENSITY |
|---|---|---|---|---|---|
| 31 | 8 ♀<br>23 ♂ | 3 yrs. (mean) | 3 out of 31 | 2½ hrs. | severe in all cases |

TABLE CONT'D

| NO. OF CASES | UNILATERAL HEADACHE | NAUSEA | FLIMMER SCOTOMA | VERTIGO | HEREDITY |
|---|---|---|---|---|---|
| 31 | 18 out of 31 | 31 out of 31 | 12 out of 31 | 6 out of 31 | 20 out of 31 |

(reference given above)

In a study of 400 adult migraine patients, it was revealed that 34% had suffered attacks before the age of 15.* These investigators concluded that childhood migraine was a much greater clinical problem than was previously believed and that psychodynamic mechanisms played an important part in the disease.

These criteria are useful in diagnosis:

Headache attacks with symptom-free intervals plus (at least two of the following) nausea, scintillating scotoma, hemicrania, and hereditary predisposition.

**For symptomatic relief in these cases, Cafergot®, N.N.R. (ergotamine with caffeine) may be administered orally. For best results, give adequate dosage promptly.**

For children within the age range 7 to 12 years—Cafergot® is administered, one tablet when the attack appears imminent followed by one additional tablet within 30 minutes. Not more than two Cafergot tablets should be administered to children within this age range.

In the adolescent age group, 12 to 18 years of age, the dosage may gradually be increased as necessary up to the usual adult dose, i.e., two tablets when the attack appears imminent followed by one tablet doses at half hour intervals until the attack is aborted. *(Total maximum dose for adults: six tablets for each attack.)*

*Katz, J., Friedman, A.P., and Gisolfi, A.: New York State J. Med. *50*: 2269 (Oct.) 1950.

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## OBITUARIES

### Herbert Raphael Mills

Dr. Herbert Raphael Mills of Tampa died at St. Joseph's Hospital in that city on June 27, 1952 after an illness of several months.

Dr. Mills was born in Albion, Mich., on Oct. 19, 1882, the son of Henry Albert and Ella Fallass Mills, both of his native state. His father, who was a talented artist, served as director of the Art School at Albion College and at DePauw University in Greencastle, Ind., and Cornell College in Mount Vernon, Iowa.

After receiving a general education in the public schools of Indiana and New York State, Dr. Mills matriculated at Cornell College in Iowa, from which he was graduated, and then attended Rush Medical College, which is now part of the University of Chicago. He received his degree of Doctor of Medicine from this institution in 1910 and the same year came to Tampa, where he became director of the local laboratory of the Florida State Board of Health, a post in which he served until the United States entered the World War. At this time he retired to enlist in the Medical Corps of the United States Army, joining this branch of the service in July 1917. He was commissioned a first lieutenant and sent overseas, where he was to serve for two years, during which time he was loaned to the British Army for five months, being identified with the 24th Royal Fusiliers and the 5th Brigade of the Royal Field Artillery. He then returned to the American forces and served with the Army of Occupation, in which he was assigned to the 1st Division in February 1918. Later he was promoted to the rank of captain and served as a field hospital officer in Germany until the summer of 1919, when he returned to the United States, being honorably discharged from the Army during the month of July of that year.

Upon resuming civilian life he returned to Tampa and re-entered his profession, specializing in pathology. In 1946, Dr. James N. Patterson, on his discharge from the Armed Forces, joined

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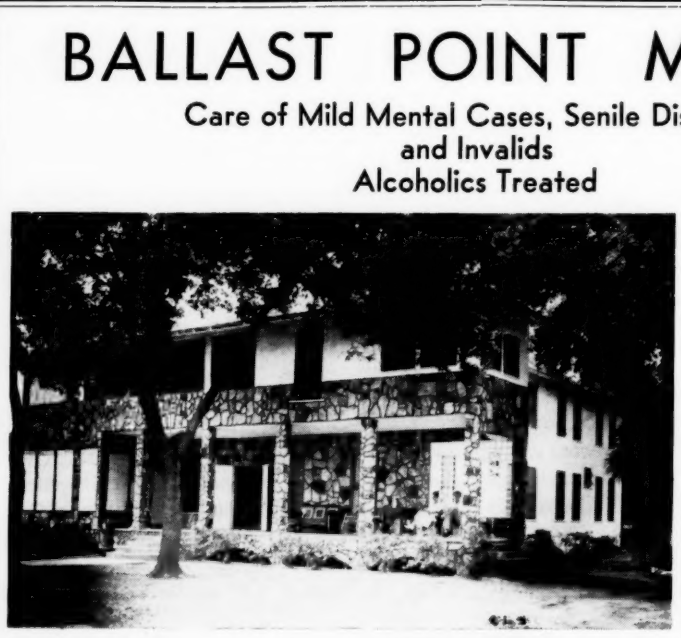

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with Dr. Mills to form the firm of Drs. Mills and Patterson. Dr. Mills was a member of the Hillsborough County Medical Association, the Florida Medical Association, the Florida Society of Pathologists and the American Medical Association. Since its inception in 1942, Dr. Mills was the Medical Director of the Southwest Florida Blood Bank. He was a Founding Fellow of the College of American Pathologists and a Fellow of the American Society of Clinical Pathologists. Dr. Mills was a Diplomate of the American Board of Pathology, being certified in both clinical pathology and pathologic anatomy. He was a member of Delta Tau Delta fraternity and Phi Beta Phi medical fraternity.

Aside from his profession, his greatest interest rested in nature and wild life. In 1946 the State Chamber of Commerce awarded him the Gold Medal of Conservation in appreciation of his outstanding work in this field. He had championed preservation and protection of all types of wild life and also done much to help the Indian population of the state. In these connections he was a member of the National Audubon Society and the Florida State Audubon Society, in which he was a member of the executive committee. Dr. Mills also belonged to the American Ornithologists Union. He was appointed by the United States Biological Survey to assist in the making of a nationwide census of ducks, the survey accomplishing much of the work by airplane. As a member of the Seminole Indian Association, he belonged to a group whose purpose it has been to help the Indian population of this state in every possible way.

Dr. Mills is survived by his widow, Marie-Louise; a son, H. Robin, who is a student at the Florida State University; and a sister, Miss Ermina M. Mills of Greencastle, Ind.

## Harold Fritz McDuffie

Dr. Harold Fritz McDuffie of Jacksonville died on March 4, 1952 in a Daytona Beach hospital. He was 61 years of age.

Dr. McDuffie was born in Fayetteville, N. C., in 1890. He received his medical training at the New York Medical College, from which he received the degree of Doctor of Medicine in 1913. He then served an internship at Flowery Branch Hospital in New York City.

Before coming to Florida to reside, Dr. McDuffie practiced medicine in Atlanta, Ga. He was a member of the staff of the Georgia Baptist Hospital and of St. Joseph's Infirmary. In 1944 he located in Jacksonville, where he specialized in ophthalmology and otolaryngology. He was a member of the Elks Club and of the Baptist Church.

Dr. McDuffie was a member of the Duval County Medical Society, the Florida Medical Association and the American Medical Association.

Surviving are the widow, Mrs. Ossie Virginia McDuffie of Jacksonville; one daughter, Miss Mary Elizabeth McDuffie of Atlanta; two stepdaughters, Miss June King and Miss Georgia King of Jacksonville; four sons, Randy Warren McDuffie of Jacksonville and Bruce McDuffie, Robert Stanley McDuffie and Harold Fritz McDuffie, Jr., all of Atlanta; and three brothers, P. C. McDuffie of Atlanta, Allen McDuffie of Asbury Park, N. J., and Morgan McDuffie of Ocean Grove, N. J.

## Errata

The correct date of the death of Dr. Arthur Jones Logie of Miami is June 13, 1952.

**Cook County Graduate School of Medicine**

ANNOUNCES COURSES FOR FALL AND WINTER 1952-1953

SURGERY—Intensive Course in Surgical Technic, Two Weeks, starting November 3, January 19, February 2. Surgical Technic, Surgical Anatomy & Clinical Surgery, Four Weeks, starting March 2. Surgical Anatomy & Clinical Surgery, Two Weeks, starting March 16. Surgery of Colon & Rectum, One Week, starting November 17, March 2. Bronchoscopy, One Week, by appointment. General Surgery, One Week, starting February 9. General Surgery, Two Weeks, starting March 30. Fractures & Traumatic Surgery, Two Weeks, starting March 2.

GYNECOLOGY—Intensive Course, Two Weeks, starting February 16. Vaginal Approach to Pelvic Surgery, One Week, starting March 2.

OBSTETRICS—Intensive Course, Two Weeks, starting November 3, March 2.

MEDICINE—Intensive General Course, Two Weeks, starting May 4. Gastroscopy & Gastroenterology, Two Weeks, starting November 3.

UROLOGY—Two Week Intensive Course starting April 27. Ten-Day Practical Course in Cystoscopy starting every two weeks.

DERMATOLOGY—Intensive Course, Two Weeks, starting May 4.

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